U. S. NAVAL AIR ENGINEERING CENTER

PHILADELPHIA, PENNSYLVANIA

Aerospace Crew Equipment Laboratory

A REPORT OF THE PHYSIOLOGICAL, PSYCHOLOGICAL, AND BACTERIOLOGICAL ASPECTS OF 20 DAYS IN FULL PRESSURE SUITS, 20 DAYS AT 27,000 FEET ON 100% OXYGEN, AND 34 DAYS OF CONFINEMENT

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ADMINISTRATIVE INFORMATION

This report is a joint effort on the part of the National Aeronautics and Space Administration, the U. S. Naval Aerospace Crew Equipment Laboratory, and the U. S. Naval Medical Research Institute, under Defense Purchase Request T-25750-G, and of the Republic Aviation Corporation, Farmingdale, Long Island, N. Y., under NASA Contract NAS-9-4172. This investigation received further support from the Bureau of Medicine and Surgery, BUMED Work Unit MF022.03.02-6001 and was authorized by the Bureau of Naval Weapons, BUWEPS WEPTASK RAE 13C 005/2001/R005 01 01, Problem Assignment No. 005RA15-25.

The principal investigator wishes to express his appreciation to the Research Groups for their efforts. Sections 3 through 12 of this report were authored by them, and the names of the responsible investigators appear on the flyleaf which heads each section.

Special mention must be made of the fine group of young officers who acted as subjects for this study. Without their absolute dedication, this study would have been impossible. They are:

LTJG James B. Abbitt, USN
CAPT Karl A. Foster, USMC
LT Kenneth C. Juergens, USN
LTJG William R. McBride, USNR
LTJG Jerry W. Munger, USN
LTJG Richard M. Pipkin, USNR
LTJG Cyrus W. Strickler III, USNR
1ST LT Carl H. Yung, USMC

We wish to express our appreciation to Professor C. J. Lambertsen, and his staff, Dr. Arthur B. DuBois, and Dr. Gordon Powers, of the University of Pennsylvania for their support and cooperation.

This technical documentary report has been reviewed and is approved.

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ABSTRACT

The study was designed to validate the 100% oxygen (258 mmHg) gaseous environment for 20 days with 7 days pre and post run evaluations. Studies include: renal and pulmonary function, retinal vascular changes, rather extensive blood work, nutrition, metabolic and water balance, bacteridlogical flora alterations, psychological manifestations, and full pressure suit and personal hygiene evaluations.

While certain significant psychological alterations were observed, the physiological studies disclosed no significant variations from normal values. The atmosphere was well tolerated; however, 20 days constant full pressure suit wear posed some special problems.

SECTION 1

GENERAL INTRODUCTION AND METHODS

CDR Kenneth R. Coburn, MSC, USN

SECTION 1

INTRODUCTION

A decision to utilize an atmosphere of 100% oxygen in United States manned spacecraft has led to intensive research in an effort to determine the partial pressure at which prolonged human exposure to this gas ceases to be of optimum value and begins to produce deleterious effects. This decision, necessitated by engineering considerations, has posed the problem of selecting an atmosphere which may be less than the best of all possible atmospheres. From an *a priori* point of view, air at approximately 760 millimeters of mercury should be the atmosphere of choice and might be eventually the most practical selection for spacecraft configurations of the future. Payload weight constraints, for example, which dictated a single gas atmosphere should diminish progressively as increasingly powerful U. S. booster vehicles in the multi-million pound thrust range become operationally available.

Nevertheless, we are posed with the original fascinating problem - at what point on a hypothetical pO_2 versus time curve does oxygen begin to limit rather than optimally sustain human physiological processes?

Many earlier studies[1-8] have produced contradictory results which require clarification. It was with this in mind that the current study was conceived; to confine six men for a period of 34 days, 20 days of which were spent at 27,000 feet on 100% oxygen and a total time in full pressure suits of 21 days with two other men to serve as sea level controls.

GENERAL METHODS

It is not the intent to describe here in any detail the specific methods employed to measure the many variables which occupied our collective interests in the several areas of concern. They are to be found in Sections 3 through 13 in the main text of this paper. In this portion the over-all aims of the study will be dealt with as will general methods used to implement the entire program.

Due to the complex nature of this investigation, it was decided by the principal investigator to utilize a simplified Program Evaluation and Review Technique (PERT) to identify events, determine critical paths and, generally, to give form to the mass of separate actions which had to be performed prior to the first experimental day. This was particularly true for two essential networks, (1) the selection and procurement of subjects and (2) the modification of the Aerospace Crew Equipment Laboratory Bio-Astronautic Test Facility into the desired double-wall configuration.

SUBJECT SELECTION

The subjects in this study were selected from a group of outstanding USN and USMC aviators who had volunteered for astronautics. This list was obtained from the U. S. Naval School of Aviation Medicine, Pensacola, Florida.[9]

The criteria for inclusion on this list were:

"a. An expressed willingness to volunteer for highly demanding technological assignments such as space flight.

b. Technical aptitude equal to or exceeding that of the Mercury Astronauts. Tests used in common with the Mercury selection program were the Minnesota Engineering Analogies Test, the Doppelt Mathematical Reasoning Test, the U. S. Navy's Mechanical Comprehension Test and the U. S. Navy's Aviation Qualification Test, In addition technical performance in naval air training was noted. Those volunteers with average or below performance records were not accepted. Each man was graded on technical aptitude as follows:

A grade of three (3) indicated that the man scored in the lower range of scores attained by the Mercury Astronauts.

A grade of two (2) indicated that the men scored in the middle range of scores attained by the Mercury Astronauts

A grade of one (1) indicated that the man equalled or exceeded the highest scores attained by the Mercury Astronauts.

It should be stressed that even the lowest range of scores, i.e., the 3's represents an ability level well above the average of the aviator population, which in turn is a superior group compared to the general population.

c. Verbal aptitude equal to or exceeding that of the Mercury Astronauts. The tests used in common with the Mercury selection program were the U. S. Navy's Aviation Qualification Test and the Miller Analogies Test. Many graduate schools use the latter for screening applicants. The same three point scale was used to describe each man with respect to the Mercury group.

d. Superior flying ability as measured by flight grades in naval aviation training. A rating of three (3) represents about average for designated aviators. A two (2) represents well above average flight grades, and a one (1) represents exceptional flight grades.

e. Rigorous physical examination with particular attention to the cardiovascular system."

Some forty officers whose names appeared on this list were contacted by letter and asked if they would be willing, to participate as subjects and, if they were willing to include anthropomorphic data to aid in determining what size full pressure suit would be required. Those officers who volunteered were sent follow-up letters and their respective commands were contacted to obtain permission to order the officers to Aerospace Crew Equipment Laboratory for the required sixty-day period. Thus, based upon their availability and the sizing data, the eight subjects were chosen.

All subjects are university graduates with degrees in science, engineering or mathematics.

Training and Orientation - During the two weeks prior to the start of the 34 day experimental period, the eight subjects received intensive training and orientation in the overall research program. This was particularly important, in view of the desire to follow the microbiological aspects of this relatively long term confinement as special sampling techniques had to be taught. Once the subjects entered their respective spaces, there was no direct contact with staff personnel except for the brief period required to obtain fundus photographs. As a result of this requirement, the subjects had to become competent in various technical procedures. These included venipuncture, pulmonary function testing, and microbial sampling of their bodies, chamber walls, and air.

This initial period was also used to obtain baseline data of a physiological and psychological nature. This included arterial punctures to determine blood pO_2, pCO_2, and pH.

Complete flight hazardous duty physical examinations were conducted by USN flight surgeons.

EXPERIMENTAL DESIGN

Six officers were selected to act as the experimental group, the remaining two comprising a small control group. The variables and the time sequence are shown in Table 1-1.

Aerospace Crew Equipment Laboratory Bioastronautics Test Facility (BATF) The interior of the large low pressure chamber was equipped with a cylindrical aluminum liner 22 feet long and 8 1/2 feet in diameter. The necessary fittings for long term, multi-manned habitation were installed as shown in Figure 1-1. Although not used in this study, provision for personal hygiene and toilet facilities were included for use in subsequent studies.

The purpose of the double-walled chamber was to insure that any gas leakage would be outboard. This was accomplished by evacuating the annulus between inner and outer walls to a pressure slightly below the 258 mmHg required. These pressures were maintained automatically as were temperature and relative humidity by MKS Baratron Meters, Type 77 and Honeywell Recorder-Controller equipment see Figure 1-2 and 1-3. Manual observer/controllers were also on constant duty.

The 100% oxygen environment was obtained from liquid derived oxygen. The atmosphere was constantly monitored by a Beckman Model F3 O_2 Analyzer, and a Beckman L/B Infra-red Analyzer, Model 15A, was used for determining CO_2. Continuous recording of O_2 and CO_2 percentages were obtained on a Minneapolis-Honeywell Continuous Drive Recorder, Model Y153X65.

Control Facility: The control facility was located adjacent to the Bioastronautics Test Facility and was essentially a plywood cottage 8 X 8 X 16 feet. The interior was furnished with equipment similar to that found in the Bioastronautics Test Facility. The layout is shown in Figure 1-4. The schedule followed by the control subjects was similar to that followed by the experimental group, with the exception of operating on a two-shift schedule.

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TABLE 1-1

EXPERIMENTAL DESIGN

Group	DAY 1-7	DAY 8-14	DAY 15-27	DAY 28-34
EXPERIMENTAL	S.L.* - No Suit	ALTITUDE** No Suit	ALTITUDE** - Suit	S.L. - Suit
CONTROL	S.L. - No Suit	S.L. - No Suit	S.L. - Suit	S.L. - Suit

* S.L. = Sea Level

** ALTITUDE - 27,000 Feet on 100% OXYGEN

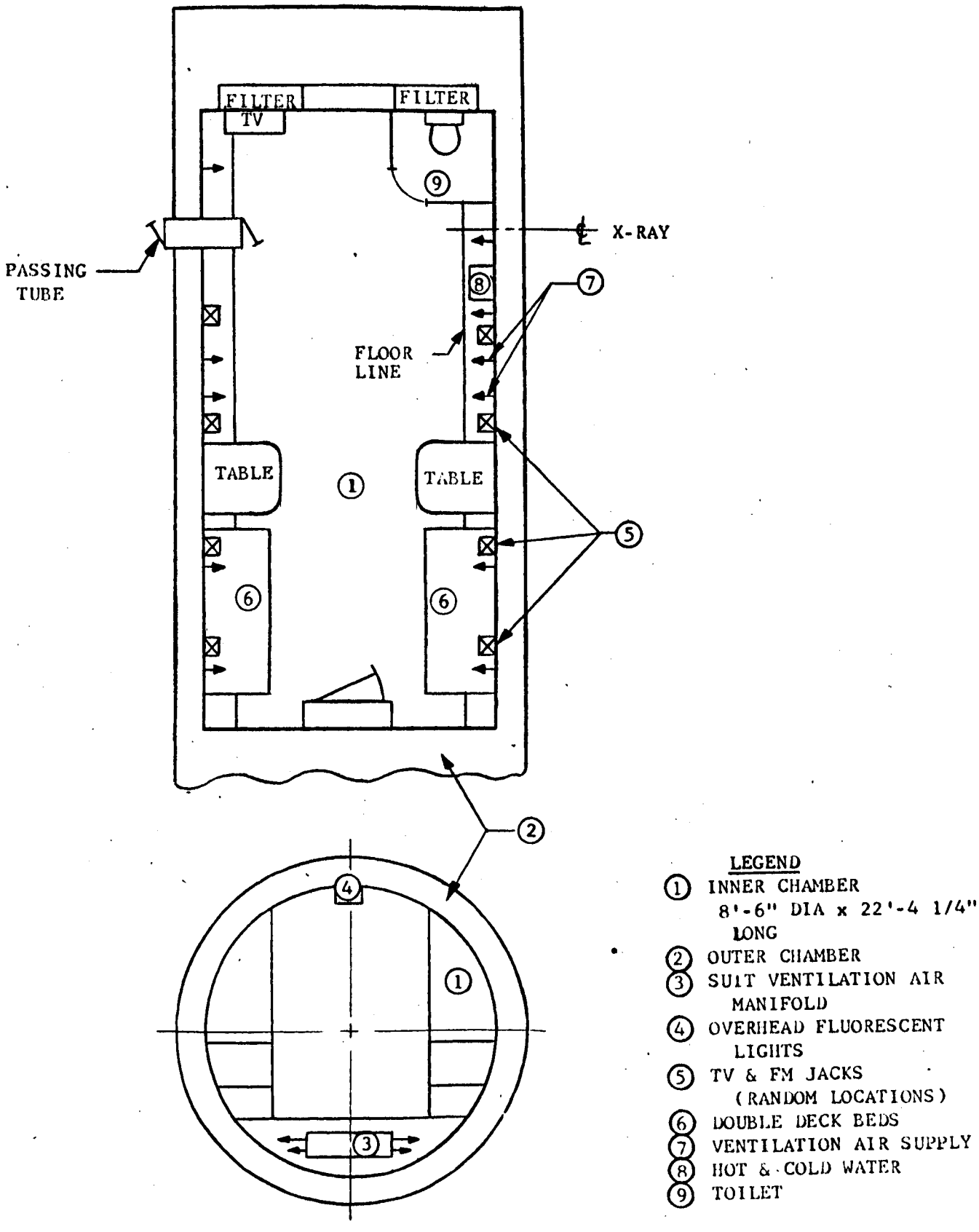

FIG. 1-1 BIOASTRONAUTICS TEST FACILITY LAYOUT

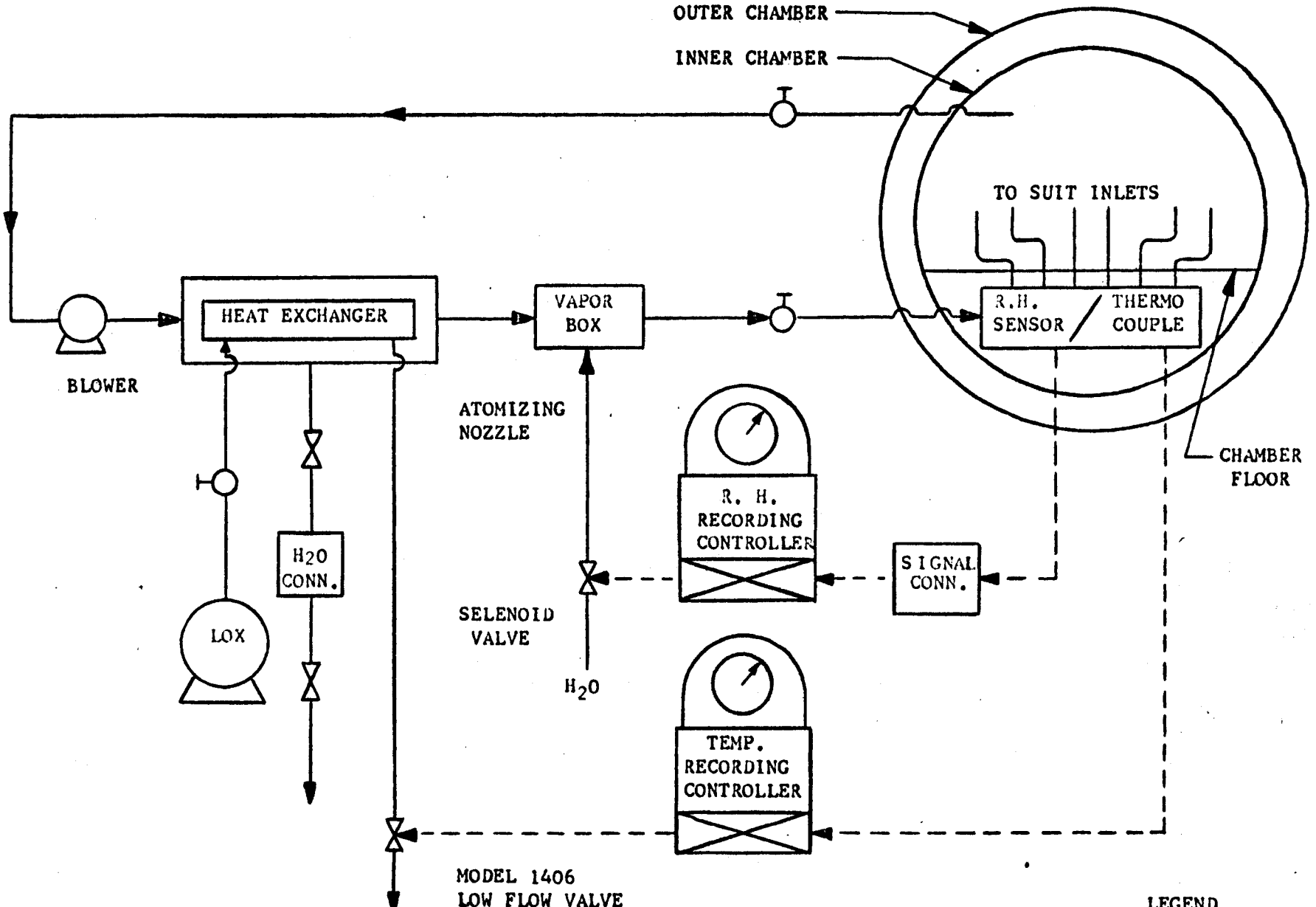

FIG. 1-2 SUIT TEMPERATURE & HUMIDITY CONTROLS SYSTEM

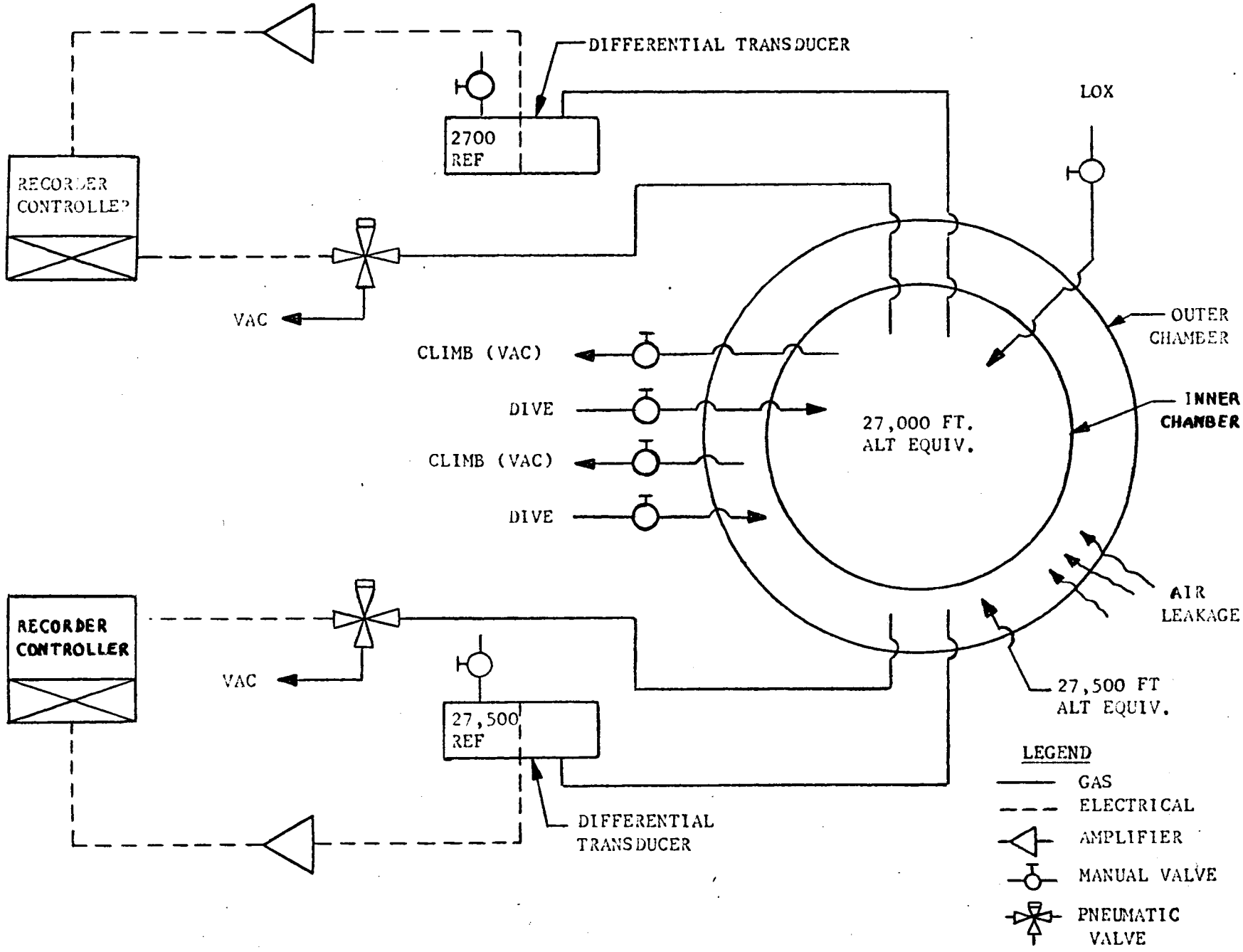

FIG. 1-3 AUTOMATIC PRESSURE CONTROL

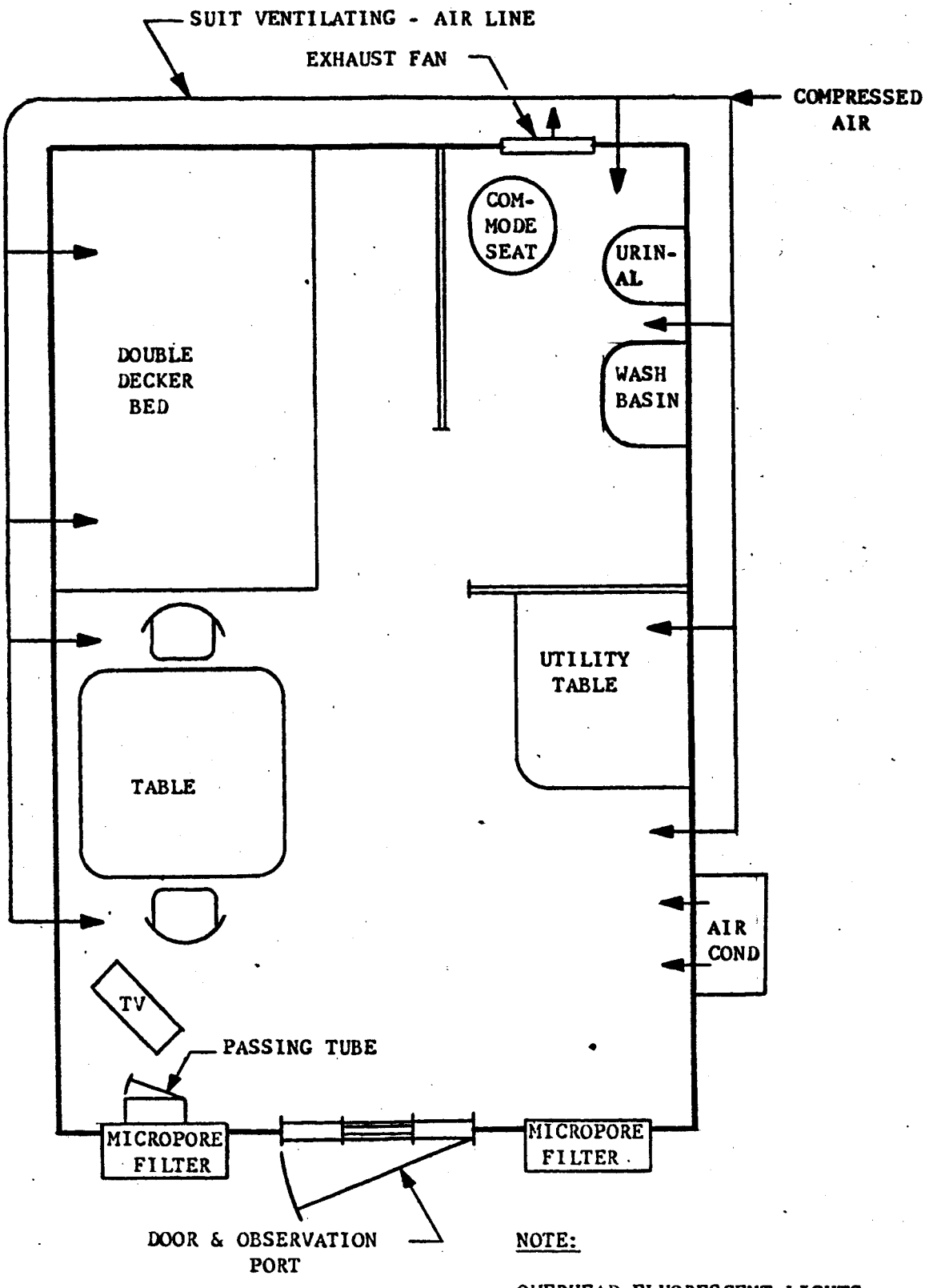

FIG. 1-4 CONTROL FACILITY LAYOUT

SECTION 2

GENERAL DISCUSSION OF RESULTS AND CONCLUSIONS

CDR Kenneth R. Coburn, MSC, USN

SECTION 2

GENERAL DISCUSSION OF RESULTS AND CONCLUSIONS

Aside from the inverse relationship between retinal blood vessel caliber and pO_2, there were no positive findings. In the case of the renal function and pulmonary function this is not surprising, as previous reports had led us to believe that none would occur as a result of our experimental design.

The wide variations noted in the creatinine levels must be ascribed to technical difficulties. Only one of the subjects showed any significant change in weight or surface area; subject 3 who deliberately although surreptitiously lost 15 pounds during the 34 days of confinement. However, the variations in creatinine excretion in this subject were no more marked than those observed in other subjects. The most probable source of error is the manner of urine collection.

Certain changes were anticipated but not observed in the case of the hematological and blood biochemistry sections. Helvey et al[1] reported changes in the blood picture of his subjects at all three pressures studied, i.e., 7.4, 5.0 and 3.8 psia. The alterations were much more apparent at 7.4 psia than at the two lower pressures of 5.0 and 3.8 psia.

Possibly the most striking change reported by Helvey et al[1] was the flattening of the peaks and shift to the left of the Price-Jones Curves. Our data indicates no such changes. In the absence of Price-Jones changes or any other alterations in blood morphology/biochemistry we can only suppose that some factor other than those anticipated was as least partially responsible for the changes noted in the Helvey study. This factor might have been mercury vapor as several mercury containing instruments were inadvertantly broken in the low pressure chamber during the course of the reported series of investigations.

The absence of significant alterations in the activities of the blood enzyme studies conducted by NMRI tend to substantiate our morphological findings. From our data, we can conclude that our experimental design produced no detectable alterations in the reduction-oxidation balance of the red blood cells. This appears to agree with A. A. Thomas[2] who has stated that a pO_2 of 300 mmHg appears to be the toxic threshold for oxygen.

The bacteriological studies indicate that although there was a general buildup of microorganisms on the bodies of the subjects and in their respective environments, this posed no special problem. However, a warning note was sounded. The isolation of Shigella Poly B, Bethesda Ballerup, and a coagulase-positive phage typeable staphlococcus, all potential pathogens, would seem to indicate a necessity for eliminating all potentially pathogenic organisms from each individual of a proposed space crew. Although there was only minimal intra-personal transfer between subjects, it must be emphasized that overt transfer can occur, and if a highly virulent strain of Shigella or Salmonella, for example, is introduced, the resulting affect could well be catastrophic in a manned spacecraft environment.

The nutritional aspect of this study is noteworthy only in that the diet was very well accepted and appeared to be adequate in all aspects.

There were no significant variations noted in the balance studies.

The psychological portion of this study, Sections 9, 9a, 10 and 11 reports changes which have significance only when related to confinement in the Bioastronautical Test Facility or control facility. No changes were noted which are considered relevent to the 100% oxygen or reduced pressure.

Some general comments arising from the debriefing session, which included both subjects and investigators, are in order. Probably the most common single source of annoyance to the subjects was the ratio of temperature/humidity. Although fairly precise control could be maintained by the automatic equipment it appears that no single set of conditions could satisfy all of the six experimental subjects for very long. There are a number of perfectly valid reasons for this.

1) The variety of suits used; i.e., USN Mark 4, USN Mark 5, NASA-MA-10 and NASA Apollo, was such that there were no common thermal characteristics. Each suit has quite different properties.

2) The suits were worn fully donned, except for the faceplate, for only about four hours a day. The remainder of the time the helmets and gloves were removed. In the case of the USN Mark 4 suits the rubber booties were cut off when moisture began to accumulate in them. All of these modifications to the various suits or the configuration in which they were worn produced a virtually insolvable problem when it came to providing not only a satisfactory temperature and humidity but in supplying vent gas flow at an optimum rate. This rate had been stipulated prior to the beginning of the run and was therefore maintained at 12 liters per minute. This was insufficient under the conditions mentioned above. Future studies of this type should provide individual control of vent gas.

Several other problems relating to the wearing of the full pressure suits arose. Sleeping presented a problem which was partially solved by "buttoning up" the suit. This not only insured optimum ventilation but, donning the helmet avoided pressure points on the neck which resulted from trying to sleep on the neck ring.

The flaking of skin and sloughing of hair has been mentioned previously but is raised again because of its pertinence in actual manned spaceflight. The flaking occurred in quantities sufficient to impair gas flow through the filters in the process of circulation and to litter the floor of the living compartment. Under weightless conditions this settling would not occur and the detritus would remain suspended in the environment.

Constant wearing of full pressure suits greatly impairs the effecting of adequate personal hygiene procedures. Although no build-up of pathogens occurred, all surfaces became markedly contaminated with coliform microorganisms. In this connection the use of the "0 Gravity Sink" did nothing to improve personal hygiene, in fact quite the opposite. Microorganism levels reached staggering proportions and the use of the "Sink" was discontinued at the end of the first week. The washcloths remained a source of contamination throughout the entire period of the run. From a purely subjective point of view the subjects' attitudes with regard to his own state of personal hygiene at the end of the 34 days varied considerably. While no one considered himself to be "clean" not all of them felt "filthy" either.

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SECTION 3

RETINAL VASCULAR RESPONSE TO OXYGEN AT INCREASED PARTIAL PRESSURES

LT Talvaris Turaids, MC, USN
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SECTION 3

RETINAL VASCULAR RESPONSE TO OXYGEN AT INCREASED PARTIAL PRESSURES

Normal retinal arteries and veins constrict when the concentration of inspired oxygen rises and dilate when it falls.[1,2] In the immature retina, vasoconstriction due to chronic hyperoxia is followed by irreversible changes, such as obliteration of the vessels.[3,4] Adults breathing 100% oxygen at sea level show a 10.5 to 37.7% decrease in the caliber of retinal vessels.[1,5] The degree of constriction, which is more marked in the veins, is substantially complete within five minutes after passing from breathing air to oxygen at one atmosphere of pressure.[5,6] At the same time, no untoward ophthalmologic symptoms or signs have developed in subjects breathing 100% oxygen at sea level for 4 to 24 hours.[6,7] However, inhalation of 100% oxygen at three atmospheres has resulted in a striking reversible impairment of vision in adults after four hours.[8] It has been suggested that the vasoconstriction in the eye in response to oxygen may serve a defensive purpose to protect the tissues from too high a concentration of oxygen.[1,9].

METHOD

A Nikon Fundus camera, using Kodak Tri-X Pan black and white film, was utilized to obtain retinal photographs of the six experimental subjects while breathing air at sea level, during the period of pre-oxygenation with 100% oxygen at sea level prior to ascent to altitude, 5 - 30 minutes after ascent to 27,000 ft on 100% oxygen, and after the subjects had been at altitude, breathing 100% oxygen for 19 days. The pupil of the test eye was dilated with tropicamide (Mydriacyl 1.0%. Alcon) prior to each study. The 35 mm film was magnified 15 times on a glass screen using an IBM Microfilm Reader, and the larger retinal vessels were measured with a caliper and steel rule with 1/64 inch divisions.

The same three arteries and veins were measured on each photograph. Easily recognizable points on both veins and arteries were selected using the optic disc or a prominent A-V crossing as a reference. The diameter of the optic disc was the same in all enlargements, thus insuring that any changes noted were not due to differences in the focus or the distance at which the pictures were taken. Mean values were obtained for the three arteries or veins measured, and the percent change from the control photographs was calculated (Table 3-1).

RESULTS AND DISCUSSION

Retinal photographs taken after the subjects had been breathing 100% oxygen at sea level for 5 to 30 minutes, show a decrease of approximately 17% in the caliber of the arteries and 20% in the veins, see Figure 3-1. Five to 30 minutes after the ascent to 27,000 ft while breathing 100% oxygen, there was only a 6 to 8% decrease in the diameter of retinal veins and arteries. This degree of decrease remained essentially the same after 19 days at altitude on 100% oxygen.

There appears to be a direct correlation of the degree of vessel constriction to the oxygen tension of arterial blood.[6,10] Smaller vessels decrease disproportionally more than larger ones,[9] and thus the original diameter of the vessel has to be considered. This may in part account for the different values of retinal vessel caliber in response to oxygen as reported by various investigators.

The decrease in the diameter of retinal vessels is directly related to the decrease in circumference, however, without further studies, it would be difficult to attempt to correlate the diameter changes with changes in vascular resistance, and hence in the blood flow. It appears that the increase in blood oxygen transport during hyperbaric oxygenation more than compensates for the reduction in retinal blood flow due to vasoconstriction. This is evidenced by the fact that the color of blood in the veins changes to approximate that of the arteries [1,10] and that hyperbaric oxygen preserves vision for long periods of time during retinal ischemia.[11,12].

Vasoconstriction in response to increased partial pressures of oxygen may not be limited to the retina. It has been demonstrated that cerebral blood flow in man decreases by about 12% when 100% oxygen is breathed at one atmosphere and up to 24% at two atmospheres pressure.[13, 14, 15] Moreover, this vascular response to hyperoxia may be a general or a systemic one. An increased arterial blood oxygen tension, even at one atmosphere, will increase peripheral vascular resistance and decrease the cardiac output and heart rate.[16,17] The stroke volume and mean blood pressure do not change, however.

CONCLUSION

The fundus oculi offers a unique opportunity for the observation of alterations in vessel caliber during changes in arterial gas tensions. Measurements from retinal photographs are a convenient way of assessing such changes. Experimental results show that both retinal arteries and veins decrease progressively in size as arterial oxygen tension is increased.

Certain questions may be raised with respect to future investigations:

1. Is there a linear relationship between the caliber of retinal blood vessels and the partial pressure of inspired oxygen?

2. Does the retina have an autoregulatory mechanism for the control of its circulation; are retinal vessels particularly sensitive to oxygen, or is vasoconstriction a general response to hyperoxia?

3. Is the vasoconstriction due to a direct response to the increase in oxygen pressure, certain metabolic changes in the tissues, or to a homeostatic mechanism to maintain tissue oxygen levels within fairly close limits and thus mitigate against possible deleterious effect of hyperbaric oxygen?

4. Is this effect due to local action of a chemical factor on the nervous cells or smooth muscle, or is the response mediated through certain neurohumeral mechanisms?

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TABLE 3-1

PER CENT CHANGE IN DIAMETER OF RETINAL ARTERIES AND VEINS BREATHING 100% OXYGEN AT SEA LEVEL AND AT SIMULATED ALTITUDE OF 27,000 FT.

	100% O_2 at sea level, 5 - 30 min	100% O_2 at 27,000 ft, 5 - 30 min	100% O_2 at 27,000 ft, 19 days
		ARTERIES	
SUBJECT			
1	-12.72%	-7.47%	-10.50%
2	-23.88%	-9.88%	-13.22%
3	-19.44%	-9.25%	- 5.55%
4	-11.42%	-2.38%	+ 2.38%
5	-13.46%	+3.03%	- 3.70%
6	-20.19%	-10.65%	- 5.12%
MEAN	-16.68%	-7.88%	- 6.74%
		VEINS	
SUBJECT			
1	-19.34%	-10.71%	- 8.92%
2	-23.88%	- 9.88%	-13.22%
3	-13.80%	- 5.12%	- 2.00%
4	-19.36%	- 5.55%	- 2.22%
5	-20.60%	- 4.60%	- 7.35%
6	-20.74%	- 5.12%	- 7.21%
MEAN	-19.55%	- 5.87%	- 5.31%

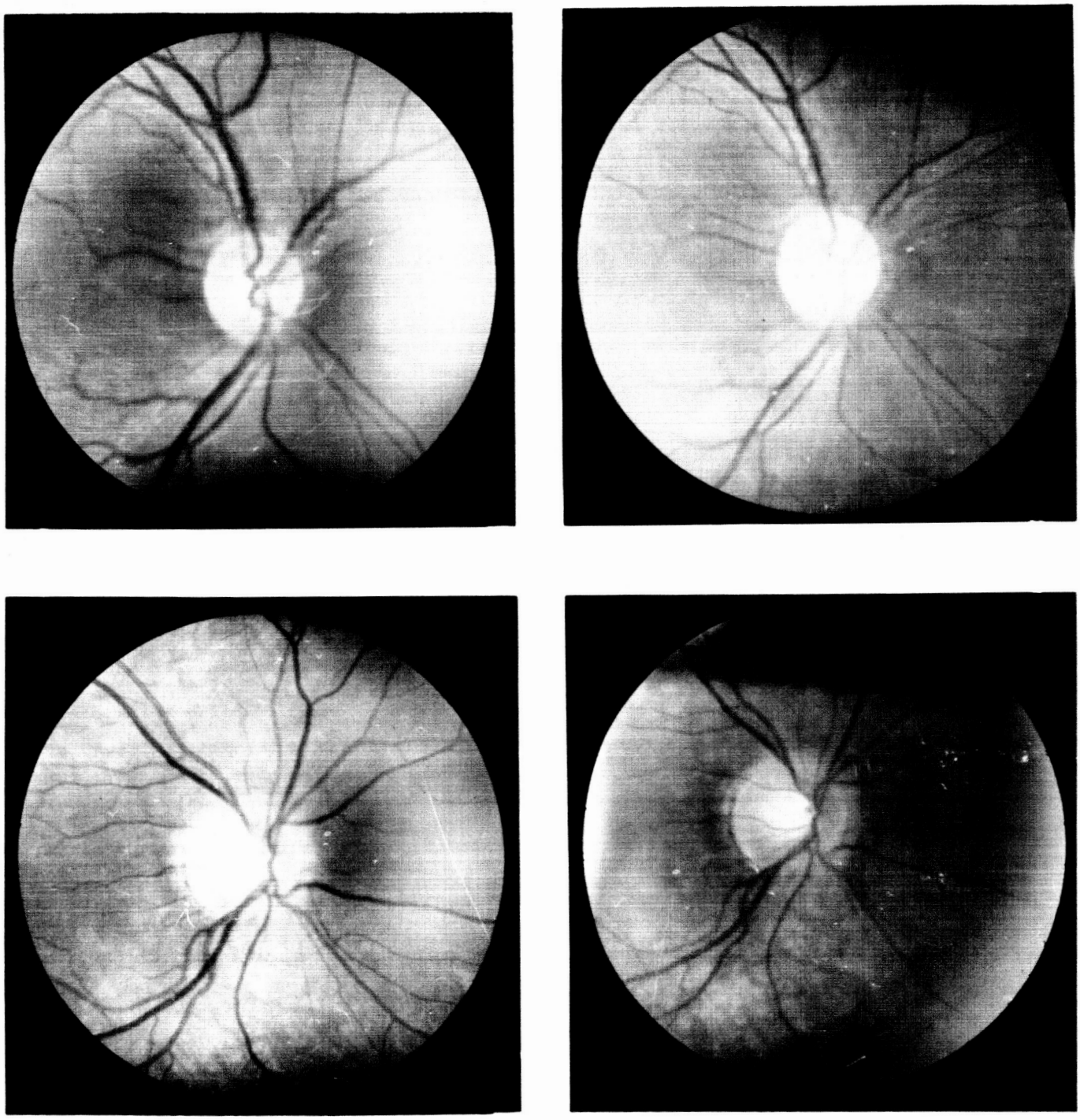

Figure 3-1 Retinal photographs of two subjects before (left) and while breathing 100% oxygen at sea level (right) showing a decrease in caliber of vessels.

PHOTO NO: CAN-371596(L)-10-65

SECTION 4

RENAL FUNCTION AND WATER BALANCE

LT Talvaris Turaids, MC, USN

SECTION 4

RENAL FUNCTION AND WATER BALANCE

Routine urinalyses, including microscopic examination, were performed periodically. Protein, sugar, and pH were determined using Hema-Combistix reagent strips manufactured by the Ames Company. When the presence of albumin was suspected from a doubtful reaction of the reagent strip, the sulfasalicylic acid turbidity test for protein was also done. Likewise, to rule out a false positive reaction for glucose, the presence or absence of the latter was also determined using Clinitest Reagent Tablets (Ames). Specific gravity was determined using an urinometer, and acetate with Acetest Tablets (Ames Company). Serum and urinary creatinine and creatinine clearance were determined once every three days. Methods used in all of the above tests were taken from standard Navy laboratory manuals published by the U. S. Naval Medical School, National Naval Medical Center, Bethesda, Md.

The subjects kept a record of their water intake and also of the volume of urine produced. These records were handled on a daily basis to provide data on water requirements. The amount of water used for personal hygiene was not recorded, however.

Urine was collected in 4000 ml polyethylene bottles and passed out through a small air lock each morning for analysis.

RESULTS AND DISCUSSION

Urinalysis data were essentially negative, with occasional white blood cells, and with no indication of red blood cells, casts, protein, sugar, or acetone. (Table 4-1).

The daily water intake and urine output data is presented in Table 4-2 and a summary of water requirements in Table 4-3. The average water usage, excluding that used for personal hygiene, was 1732 ml per man per day. The average water available to the body from all sources including preformed water in the food and water of oxidation was 2048 ml per day. Water excreted from the kidneys and in feces averaged 1110 ml/man/day. Assuming that the subjects were in a state of normal water balance, the difference between the water available to the body and the water excreted will be the insensible loss of 938 ml/man/day. Insensible loss at sea level has been estimated to be on the order of 900 ml/day. [1,2] These data are also in good agreement with previously published studies. [3,4]

Table 4-4 presents the data on serum and urinary creatinine and creatinine clearance. The values were found to vary excessively from day to day and the accuracy of the data is questionable. Several factors may account for this: 1)The subjects in drawing their own blood frequently produced hemolysis, 2)No preservative was used in the urine as it would have interfered with other chemical determinations. 3)On several occasions the subjects used urine bottles other than their own, 4)The urine samples collected in the mornings were not necessarily exactly 24 hour specimens. Any or all of the above may have influenced the creatinine concentration and hence its clearance. Thus, no conclusions can be drawn about this aspect of body metabolism or kidney function.

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(4) Welch, B. E., Morgan, T. E., and Ulvedal, F.: Observation in the SAM Two-Man Space Cabin Simulator. Aerospace Med. 32:583, 1961.

Table 4-1 SUMMARY OF URINALYSIS DATA *

Day		Subject 1	2	3	4	5	6	7	8
2	Spec. grav.	1.031	1.028	1.030	1.022	1.025	1.021	1.029	1.032
	Microscopic	neg	0-2 WBC	0-2 WBC	neg	0-2 WBC	neg	neg	3-4 WBC
3	Spec. grav.	1.027	1.024	1.024	1.021	1.023	1.014	1.025	1.030
	Microscopic	2-3 WBC	0-2 WBC	neg	0-2 WBC	0-2 WBC	neg	0-2 WBC	2-4 WBC
5	Spec. grav.	1.030	1.032	1.032	1.025	1.028	1.015	1.037	1.035
	Microscopic	2-3 WBC	2-3 WBC	0-2 WBC	0-2 WBC	0-2 WBC	neg	neg	2-4 WBC
11	Spec. grav.	1.027	1.025	1.022	1.013	1.027	1.027	1.029	1.029
	Microscopic	1-2 WBC	neg	0-1 WBC	0-2 WBC	0-1 WBC	neg	0-2 WBC	2-3 WBC
20	Spec. grav.	1.029	1.023	1.028	1.015	1.030	1.030	1.032	1.030
	Microscopic	2-5 WBC	0-2 WBC	0-1 WBC	0-2 WBC	0-1 WBC	0-1 WBC	neg	1-2 WBC
22	Spec. grav.	1,028	1.025	1.028	1.015	1.030	1.030	1.031	1.030
	Microscopic	0-2 WBC	0-2 WBC	0-2 WBC	neg	neg	neg	neg	neg
23	Spec. grav.	1.025	1.024	1.027	1.027	1.027	1.027	1.030	1.022
	Microscopic	0-1 WBC	0-2 WBC	1-2 WBC	0-1 WBC	0-1 WBC	neg	neg	neg
24	Spec grav.	1.028	1.028	1.030	1.015	1.025	1.021	1.031	1.032
	Microscopic	0-2 WBC	2-3 WBC	neg	neg	neg	neg	0-2 WBC	neg
25	Spec. grav.	1.025	1.024	1.030	1.015	1.025	1.030	1.030	1.024
	Microscopic	1-2 WBC	12-14WBC	0-1 WBC	neg	neg	2-4 WBC	1-3 WBC	neg
26	Spec. grav.	1.030	1.025	1.032	1.020	1.022	1.027	1.032	1.025
	Microscopic	3-4 WBC	5-6 WBC	neg	neg	neg	neg	2-3 WBC	neg
27	Spec. grav.	1.027	1.020	1.025	1.010	1.020	1.030	1.030	1.025
	Microscopic	4-6 WBC	neg	0-1 WBC	neg	neg	neg	neg	neg
28	Spec. grav.	1.028	1.020	1.025	1.010	1.022	1.028	1.030	1.025
	Microscopic	2-4 WBC	neg	neg	neg	2-3 WBC	0-2 WBC	neg	2-4 WBC
29	Spec grav.	1.026	1.026	1.020	1.020	1.024	1.026	1.024	1.020
	Microscopic	0-2 WBC	0-2 WBC	neg	0-3 WBC	neg	0-2 WBC	2-3 WBC	0-1 WBC
31	Spec. grav.	1.025	1.021	1.025	1.011	1.019	1.025	1.028	1.025
	Microscopic	0-1 WBC	0-1 WBC	3-4 WBC	1-2 WBC	0-1 WBC	0-1 WBC	1-2 WBC	0-2 WBC
33	Spec. grav.	1.023	1.017	1.024	1.013	1.019	1.016	1.028	1.026
	Microscopic	neg	neg	neg	neg	neg	neg	neg	neg
34	Spec. grav.	1.025	1.020	1.025	1.012	1.020	1.020	1.026	1.023
	Microscopic	neg	0-1 WBC	0-2 WBC	neg	0-2 WBC	neg	0-2 WBC	neg

* There was no indication of casts, protein, sugar, acetone, or red blood cells. Reaction was acid in all cases.

Table 4-2 DAILY WATER INTAKE AND URINE OUTPUT (ml/day)

Day		Subject 1	2	3	4	5	6	7	8	Mean
1	Intake	1491	1388	1347	2109	1375	1811	1021	1326	1483
	Output	900	1020	900	1740	680	1120	1220	1200	1098
2	Intake	1641	1633	1573	2363	1966	1804	1574	1967	1815
	Output	920	980	980	1400	1100	2120	1080	850	1179
3	Intake	2152	1697	1402	2582	1878	2407	1588	2445	2018
	Output	900	1300	1100	1400	1100	1200	920	520	1055
4	Intake	1784	1536	1616	2500	1887	2131	1503	1786	1842
	Output	740	740	740	1980	1580	1650	720	880	1116
5	Intake	1584	1699	1517	2146	1851	2747	1786	1772	1887
	Output	810	1170	1040	1230	920	1340	1020	995	1065
6	Intake	1532	1804	1403	2778	1704	2017	1432	2111	1847
	Output	1120	1140	920	1440	1120	1600	740	860	1122
7	Intake	1593	1783	2069	2443	1789	2583	1673	2411	2043
	Output	1000	940	1000	1480	1040	1460	540	940	1050
8	Intake	1844	1844	1531	2276	1777	2009	1134	1584	1749
	Output	650	1000	640	1240	800	1370	730	790	903
9	Intake	1778	1770	1077	2053	1783	2002	1375	1657	1686
	Output	770	1160	880	2330	880	1002	1000	1000	1130
10	Intake	2081	2471	1687	2276	1721	1928	1758	2187	2013
	Output	900	850	820	1250	1160	1080	660	600	915
11	Intake	2092	1693	1660	1963	1886	1632	1616	2114	1832
	Output	1100	960	820	1120	1020	960	1040	1180	1025
12	Intake	1770	1633	1418	1856	1806	2073	1333	1619	1688
	Output	900	1460	780	1000	1020	1240	800	940	1017
13	Intake	1804	1748	1517	2066	1874	1831	1318	1574	1716
	Output	960	980	740	1000	1060	1260	800	780	947
14	Intake	1741	1911	1304	2365	2143	2349	1063	2001	1859
	Output	1060	1050	740	1280	940	1040	840	900	981
15	Intake	1900	1845	1758	2265	1609	2021	1346	1268	1751
,	Output	900	1020	480	1820	1080	1180	1040	820	1042

Table 4-2 (Continued)

Day		1	2	3	4	5	6	7	8	Mean
16	Intake	1808	1602	1588	2315	2113	1321	1389	1618	1817
	Output	980	1020	800	1600	1220	860	880	800	1030
17	Intake	1528	1819	1120	2234	1846	1896	1431	1535	1676
	Output	860	970	620	1280	1280	1020	780	980	973
18	Intake	1795	1881	1658	2433	2095	1836	1361	2020	1884
	Output	1020	900	700	1760	1040	1600	640	700	1045
19	Intake	1867	2132	1148	2463	1826	1523	1672	904	1691
	Output	1040	800	660	1860	1180	1000	740	800	1010
20	Intake	1663	1641	907	3257	1990	1191	1503	1744	1737
	Output	800	540	620	2300	1540	1120	1020	700	1080
21	Intake	1663	1586	1630	2435	1927	1376	950	1677	1655
	Output	840	1000	480	1940	880	420	800	700	882
22	Intake	2137	2013	907	2719	2242	1713	1431	2026	1898
	Output	1080	960	570	1360	1180	960	580	920	951
23	Intake	1557	1669	1148	2663	1815	1588	1361	1380	1647
	Output	1160	1320	720	3120	1880	1080	1000	720	1375
24	Intake	1649	1388	655	1949	2127	1647	1021	1595	1503
	Output	900	1140	570	1820	1460	820	740	920	1046
25	Intake	1518	1709	1418	1782	2003	1251	1119	1634	1554
	Output	880	1060	500	1560	920	1160	740	900	965
26	Intake	1755	1638	1077	3143	2208	1231	1404	1433	1736
	Output	1100	1340	660	2220	1380	1200	680	920	1187
27	Intake	1448	2028	1389	2492	1944	2017	1517	1411	1780
	Output	1040	1320	600	1780	1280	980	920	900	1100
28	Intake	1351	1401	1191	2006	2064	1385	1134	1789	1540
	Output	1300	1640	700	2440	2240	1420	800	940	1435
29	Intake	1535	1534	780	2577	2038	1545	1077	1167	1531
	Output	1300	1160	600	2180	1240	1300	760	760	1162
30	Intake	1541	1716	1531	2321	2010	1560	1262	2294	1779
	Output	1100	1400	590	2440	1360	880	940	960	1207

Table 4-2 (Continued)

Day		Subjects 1	2	3	4	5	6	7	8	Mean
31	Intake	1438	1419	824	2822	1975	1588	1432	1611	1638
	Output	1100	1340	720	2300	1560	980	900	840	1217
32	Intake	1310	1507	1304	2348	2072	1547	1134	1619	1605
	Output	1020	1280	580	2200	1920	1180	700	960	1230
33	Intake	1239	1697	913	3789	1981	1396	1474	1129	1702
	Output	840	1080	660	2000	1220	1400	720	1060	1112
34	Intake	1647	1913	1262	707	1924	2383	1163	1334	1541
	Output	1080	1280	600	2375	1200	1400	720	620	1159
Mean intake		1676	1728	1344	2331	1919	1805	1366	1692	1732
Mean output		972	1097	721	1773	1217	1188	829	866	1082

Table 4-3 SUMMARY OF WATER DATA*

	Subjects							
	1	2	3	4	5	6	7	8
Liquids (ml/day)	1084	1166	944	1623	1313	1338	890	1215
Food rehydration	588	562	400	708	606	467	476	477
Water in food	16	16	16	16	16	16	16	16
Water of oxidation	300	300	300	3300	300	300	300	300
Total water available	1988	2044	1660	2647	2235	2121	1682	2008
Water excreted	1003	1117	752	1795	1248	1216	856	892
Urine	972	1097	721	1773	1217	1188	829	866
Feces	31	20	31	22	31	28	27	26
Evaporative water loss	986	927	908	852	987	905	826	1116

* Daily Averages

Table 4-4 SERUM AND URINARY CREATININE AND CREATININE CLEARANCE

Day		Subject 1	2	3	4	5	6	7	8	Mean
5	Serum creatinine (mg%)	0.78	1.00	1.00	1.16	0.78	0.78	1.00	0.78	0.91
	Urine creatinine (mg%)	100	70	260	160	180	120	220	90	150
	Creatinine clearance (ml/min)	73	55	159	113	240	145	220	79	135
9	Serum creatinine	1.21	1.38	0.92	1.05	1.43	1.43	1.55	2.61	1.44
	Urine creatinine	277	262	388	225	155	300	347	274	278
	Creatinine clearance	125	157	77	351	67	154	86	72	136
12	Serum creatinine	1.00	1.32	1.44	0.80	0.92	1.44	0.92	1.44	1.16
	Urine clearance	143	195	207	143	132	143	249	201	176
	Creatinine clearance	90	148	143	124	102	87	148	89	116
15	Serum creatinine	1.16	1.16	1.40	1.00	1.32	1.16	1.24	1.44	1.23
	Urine creatinine	201	178		100	132		144	249	167
	Creatinine clearance	114	108		161	75		66	83	101
18	Serum creatinine	1.10	1.32	2.00	1.55	1.00	1.43		1.21	1.37
	Urine creatinine	146	137	166	76	137	76	166	128	129
	Creatinine clearance	98	124	40	63	100	56		56	77
21	Serum creatinine	1.32	1.44	1.66	1.22	1.44	1.44	1.66	1.32	1.43
	Urine creatinine	249	247	273	121	165	237	166	286	218
	Creatinine clearance	107	113	54	128	69	57	43	101	84
24	Serum creatinine	1.25	1.34	1.16	1.43	1.45	1.61	1.61	1.25	1.38
	Urine creatinine	201	328	273	121	121	201	202	95	192
	Creatinine clearance	100	186	64	102	81	68	67	49	89
27	Serum creatinine	1.40	1.40	1.61	2.04	0.85	2.60	1.61	1.61	1.64
	Urine creatinine	189	166	274	121	144	178	212	237	190
	Creatinine clearance	97	108	70	70	150	48	104	88	91
30	Serum creatinine	1.32	1.43	1.00	1.10	0.95	1.10	1.30	1.21	1.17
	Urine creatinine	110	80	154	40	35	121	110	143	99
	Creatinine clearance	62	53	62	57	40	67	104	77	65
35	Serum creatinine	1.00	1.00	0.70	0.90	1.32	2.00	1.10	1.00	1.12
	Urine creatinine	70	132	161	100	143	110	236	286	154
	Creatinine clearance	57	132	159	199	97	85	95	134	119

SECTION 5

BLOOD STUDIES

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SECTION 5

BLOOD STUDIES

INTRODUCTION

The problem of oxygen toxicity is well known and has been studied since the days of Priestley. However, there are conflicting opinions with regard to the toxic effect of this gas upon red blood cells. Early reports indicated that increased partial pressures of oxygen could be breathed with no deleterious effect upon the blood. Clamann and Becker-Freyseng[1] reported in 1939 that two subjects breathing 0.9 atmospheres oxygen (578 mm Hg) for 65 hours showed no change in erythrocyte count, however the average hemoglobin fell from 17.3 grams to 16.2 grams on day two and then returned to 17.2 grams on day three. In 1947 Ohlsson[2] found no changes in the formed blood elements, except for a rise in the WBC from 7,600 to 12,000 cell/mm^3 in one subject following exposure to 78-88% oxygen at 1 atmosphere for about 55 hours.

In contrast, Tinsley et al.[3], in 1949, noted that when normal subjects were given 50% to 100% oxygen by mask at 1 atmosphere, small but significant decreases in red blood cell count and hemoglobin were noted during the first few days of the experiment. These values remained depressed until air breathing was resumed. Reticulocyte count fell by 1/3 and radio-iron uptake was reduced during the period of oxygen administration.

With concern over oxygen toxicity to the red blood cell established, two major theories have evolved in explanation for the possible mechanism. These are hemolysis due to oxidation, and bone marrow suppression due to lowered erythropoietin levels. The first theory has much experimental and theoretical support. Jandl et al.[4], in 1960, showed that incubation of red cells in vitro under high concentrations of oxygen caused hemolysis accompanied by changes similar to those seen in Heinz body anemias. It is also known that certain individuals with a deficiency of glucose-6 phosphate dehydrogenase in their red cells may develop severe hemolytic episodes following ingestion of oxidizing drugs such as primaquine. In theory, the red blood cells of the body may have adapted to withstand that partial pressure of oxygen experienced by man in his normal range of environments. If this delicately balanced arrangement were upset, either by an increase in oxygen or a reduction in the enzyme, hemolysis could occur.

The theory of bone marrow suppression is more difficult to support. It is known that reduced oxygen tension causes a rise in blood erythropoietin levels with a resulting secondary polycythemia. From this, it would seem that erythropoietin production may be regulated by blood oxygen saturation, and increased oxygen might reduce the erythropoietin output of the kidney. Gyllensten and Swaubeck[5] may have substantiated this with an experiment reported in 1959. They found that in growing mice, exposure to high concentrations of oxygen damages the erythrocyte-producing

or regulating mechanisms with subsequent changes in the circulating blood after a "free interval" with apparently normal blood findings.

It therefore appears that there is considerable variation of opinion as to the effect of increased oxygen tension upon the red blood cell and, if there is an effect, by what mechanism it is brought about. With this in mind, there was obviously reasonable concern when a one gas system was decided upon for our spacecraft atmospheres as future efforts would require long exposures to it.

We must emphasize that although our atmosphere is 100% oxygen, our results cannot be compared with early experiments done at similar concentrations at sea level. Two hundred fifty eight mmHg of oxygen represents 163 mmHg oxygen in the alveolus, according to the alveolar equation. This is an increase of only 62 mmHg over the oxygen pressure in the alveolus which results from breathing ambient air at sea level. Although reduced total pressure and lack of nitrogen must also be considered as variables, comparison will be made to prior studies only on the basis of the effective partial pressure of oxygen.

Recent studies using increased partial pressures of oxygen along with reduction in total pressure have shown essentially no effect upon the red cell. Michel et al.[6] noted that hemograms done on six subjects exposed to 80% oxygen at an altitude of 10,000 feet for seven days were within normal limits. More recently, Hall and Martin[4] demonstrated that a subject could tolerate 3.5 psi on 100% oxygen for 72 hours with no abnormal changes in the hematologic studies. These experiments were of relatively short duration and at altitudes different than those used in this study.

Two recent, long duration experiments have been performed using 27,000 feet altitude. Zalusky et al.[8] exposed four of eight subjects to a total pressure of 258 mmHg at 98.5% oxygen and 0.2% nitrogen and four subjects to a total pressure of 700 mmHg at 33% oxygen and 62.3% nitrogen for a period of 30 days. Except for slight changes in red cell values and a hematocrit reduction of 6.7% and 9.1% in the 258 mmHg group and the 700 mmHg group, respectively, most of the results of the hematopoietic studies were normal. His conclusion was that it appeared "30 days exposure to the increased oxygen partial pressures used in this study does not significantly alter hematopoiesis." A study carried out by Helvey[9] in 1963 showed quite different results. In this study, twenty eight men were divided into four groups and placed for fourteen days in a sealed chamber at sea level (control), 7.4 psi (380 mmHg; 18,000 feet), 5 psi (258 mmHg; 27,000 feet), 3.8 psi (196 mmHg; 33,000 ft.). The hematologic findings are most striking and appear in the following author's summary.

Summary of Data

"The 5.0 psi group (except Subject 35) demonstrated a slight anemia, microcytosis, increased osmotic fragility, and minimal erythroid hyperactivity. Subject 37 had a loss of over 2.0 gm% hemoglobin and a 2.2% reticulocyte count. The follow up examinations nine and eleven weeks post-run more clearly demonstrated that the hematological abnormalities of the subject had persisted. The Price-Jones curve continued to show flattening and broadening of the base with a concomitant microcytosis. The morphology of the red blood cells showed the following abnormalities: anisocytosis, spherocytosis, abnormal distribution of hemoglobin, stippled cells, polychromasia, normoblasts, Howell-Jolly bodies and Cabot's ring cells. Additionally, there was a 2.1 gm% decrease in mean hemoglobin nine weeks post-run, followed by a 0.8 gm% increase in hemoglobin concentration with a 3% reticulocyte response eleven weeks post-run. Subject 35 (later shown to have thalassemia trait) demonstrated a hemolytic anemia with a progressive decrease in hemoglobin from 15.8 to 10.5 gm%. Post-run examinations indicate that his blood picture appears to have stabilized between 12 to 13 gm% hemoglobin with a continued abnormal morphological picture consistent with his hereditary hemoglobin defect (thalassemia trait)"[9].

Obviously, the contradictory results of the preceeding studies indicates the need for a clear and intensive study of the problem before manned spacecraft can be planned for long duration experiments utilizing the 100% oxygen environment.

METHODS AND MATERIALS

A series of hematologic studies were performed with the primary purpose of determining if there was any change in the rate of red blood cell production or destruction. These included a complete blood count, red cell indices, reticulocyte count, Price-Jones curves, osmotic and mechanical fragilities, and direct and indirect bilirubin. Blood enzyme activity is reported separately in Section 6. The blood for analysis was drawn by venipuncture approximately every third day with an effort made to get as close as possible to the beginning and end of each set of conditions during the run. For uniformity, no food was eaten for six hours prior to each blood letting. Eleven ml. of blood were taken at each sampling.

Subjects were trained over a period of two weeks to perform venipunctures on each other. In this manner, sampling could be taken during the study without the necessity of moving personnel in and out of the chamber. Twenty-one gauge needles were used for the drawing and were removed from the syringe before expelling the blood down the walls of the collecting tubes.

The complete blood count and red cell indices were performed in the standard manner using a Max Levy counting chamber with the improved Neubauer ruling. Differential slides were stained with Wright's solution. Hemoglobin was determined by the cyanmethemoglobin method using the Klett-Summerson colorimeter. The microhematocrit determination was used.

Reticulocyte counts were made using the Hartman-Leddan methylene blue reticulocyte stain. Price-Jones curves were drawn by measuring the diameters of 200 red cells through an Okular-Schraubernikrometer to the nearest 0.1 micron. Curves were then made by connecting the peaks of columns of cells in each category. Osmotic fragility was measured by monitoring beginning and complete hemolysis after two hours of standing in tubes containing salt solutions ranging from 0.5% to 0.24%. Mechanical fragility was done using 1 ml of blood in 7.5 ml stoppered test tubes containing 50 glass beads of 4 mm diameter which were then agitated on a pipette shaker at 270 strokes per minute with a stroke distance of two inches for a period of five minutes. Before and after microhematocrits indicated the drop in hematocrit due to breakdown of red cells. A time sufficient to cause a 3% drop was selected in order that any increased tendency toward mechanical hemolysis would become apparent. Direct and indirect bilirubin determinations were made with the diazo technique using a Beckman Spectrophotometer.

RESULTS

As seen in Figure 5-1, the averaged hematocrit of the subjects varied no more than 2.5 percent throughout the entire run. The controls are noted to maintain an almost constant elevation of approximately 2.5 mm above that of the subjects, however this elevation was established prior to the beginning of the test atmosphere, and did not change appreciably throughout the remainder of the run.

The red blood cell (Fig. 5-2) count is seen to correspond closely to the graph of the hematocrit. Here again, essentially no change was seen in the subjects before and after exposure to the test atmosphere, nor is there any change in their relationship to the controls during this period. It must be noted at this time that the slight elevation of the controls in both of these graphs is the result of the exceptionally high readings of one control subject. The other control subject maintained readings almost identical to those of the six experimental subjects.

The hemoglobin concentration (Fig. 5-3) showed an initial climb which was roughly parallel between subjects and controls during the first week of confinement. This climb leveled off in the control group at the end of the first week and maintained a range between 16.5 and 17.5 grams percent. There was an abrupt drop in the subject's hemoglobin concentration back to pre-run levels following the onset of the test atmosphere with a moderate rise again during the week following a return to sea level conditions.

The difference seen between the two groups is due primarily to the same subject as mentioned previously. The other control subject also maintained somewhat higher values during that portion of the run. It must be noted that although the values for the experimental subjects were below the control subjects, all values were within normal limits and never dropped below pre-run levels.

From the preceeding data the red blood cell indices were calculated. These include the mean corpuscular hemoglobin concentration,(Fig. 5-4), mean corpuscular hemoglobin (Fig. 5-5) and mean corpuscular volume.(Fig. 5-6). These data show that the slight change observed appears to be in the hemoglobin content of the cells. A relatively small increase was noted in the control subjects.

The white blood count (Fig. 5-7) varied greatly, but remained within normal limits for all subjects for the duration of the run. Essentially no difference was noted between the two groups, nor between the values of the pre, during, or post exposure determinations.

The reticulocyte count(Fig. 5-8)remained within normal limits throughout the entire run for both groups with no subject reaching as high as two percent. There was a very slight rise in both groups during the exposure period, but this could tend to indicate a variation in laboratory technique rather than a significant change.

Price-Jones curves (Fig. 5-9, 5-10) were compared and evaluated as to height of the mean and the lateral spread. These varied only slightly and the curves were shown to maintain essentially their initial shape throughout the run for both groups.

Beginning and complete hemolysis for the osmotic fragility test (Fig. 5-11) was almost identical for both groups and, again, no change was seen before and after exposure to the test atmosphere.

The fall in hematocrit due to mechanical fragility (Fig. 5-12) accelerated slightly in both groups throughout the run. In the experimental group it amounted to four %. the day following descent to sea level. Because of the minimal degree of change, and because the control and experimental group so closely approximated each other, it is felt that this change fails to demonstrate increased mechanical fragility of the red cell.

It is interesting to note that although the increase in mechanical fragility on the thirtieth day is very slight, small changes occurred on this date in several other tests. There was a slight drop in the subjects' mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and reticulocyte count. There was a slight rise in red blood cell count. These changes are listed only to make note of them, for it is felt that they are so small and contrast so poorly with the control group that they are of no significance.

Indirect bilirubin (Fig. 5-13) was calculated by subtracting direct from total bilirubin (Fig. 5-14). Fluctuations were greatest in the control group. The experimental group maintained a generally lower indirect bilirubin with no evidence of change during the experimental period.

DISCUSSION

From previously published reports relating to hematologic data, our interest was directed toward the toxic effects of oxygen only upon the red blood cell. To investigate these effects, three parameters were measured. These were the red cell itself, the breakdown products and what, if any, response the protective mechanisms made.

The red blood cell was studied for change in size by means of the mean corpuscular volume and the Price-Jones curves. Since red blood cells decrease in size up to maturity, a release of immature red cells from the marrow could be shown in this manner. Another test indicating changes in the blood forming mechanisms is the reticulocyte count. Reticulocytes are immature red cells containing a net-work of filaments or granules. Since these granulofilamentous substances remain demonstrable for a few days after the erythrocytes are delivered to the peripheral blood, the reticulocyte count is employed as a measure of the physiological activity of the bone marrow.[10]

Our data show no indication of change in the activity of bone marrow. The height, width and mean peaks of the Price-Jones curves of the experimental group show essentially no change throughout the experiment. The control group showed greater variation, but this is to be expected due to the smaller sample.

The mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, hematocrit and hemoglobin are all means of studying possible changes in the nature of the circulating red cell. These are of special interest in that there was no significant decrease in any of these values. Although an unexplained increase in hemoglobin occured in the controls, especially in one subject it must be conceded that no appreciable change in the status of the circulating red cells occurred. The white blood cell count tends to verify that there was no concentration or dilution of the blood cell mass.

If there were an increase in red cell aging as in glucose-6-phosphate dehydrogenase deficiency, an increase in red cell fragility might be expected. The small, but consistant rise in mechanical fragility is of some concern. However, the similarity of the curves of the experimentals and the controls makes it seem that technique variations are responsible and that nothing here indicates increased fragility as a result of the conditions imposed.

The bilirubin, both indirect and total, would show an increase if the hemolysis of red cells was so great that the liver could not clear the breakdown products. Although variations due to technique are high in this test, it is safe to say that hemolysis, if it occurred, was within the capacity of the liver to clear it.

Finally, the protective mechanism using glucose-6-phosphate dehydrogenase was not affected at all during the experiment. This is not a proof that no protective efforts are being carried out as a defense against oxidation, but rather, a demonstration that no change does occur in the one known enzyme system whose deficiency can cause a hemolytic anemia.

CONCLUSION

There have now been three separate studies under essentially the same environmental conditions, i.e. 100% oxygen at 27,000 foot simulated altitude for extended periods of time. From the findings of this study it appears that essentially none of the hematologic changes, such as those reported in the Republic experiment, were found of particular interest in that experiment, was the large number of mercury containing instruments broken inside the chamber. These included six oral thermometers, and two sling psychrometers. Since stippled red cells were noted, it is of special concern that a toxic agent such as mercury vapor may have been involved.

With this in mind, and since our findings so well agree with the work done by Zaluskey[7], it is felt that this environment can be accepted by man for at least twenty days with no deleterious effect upon the red blood cell.

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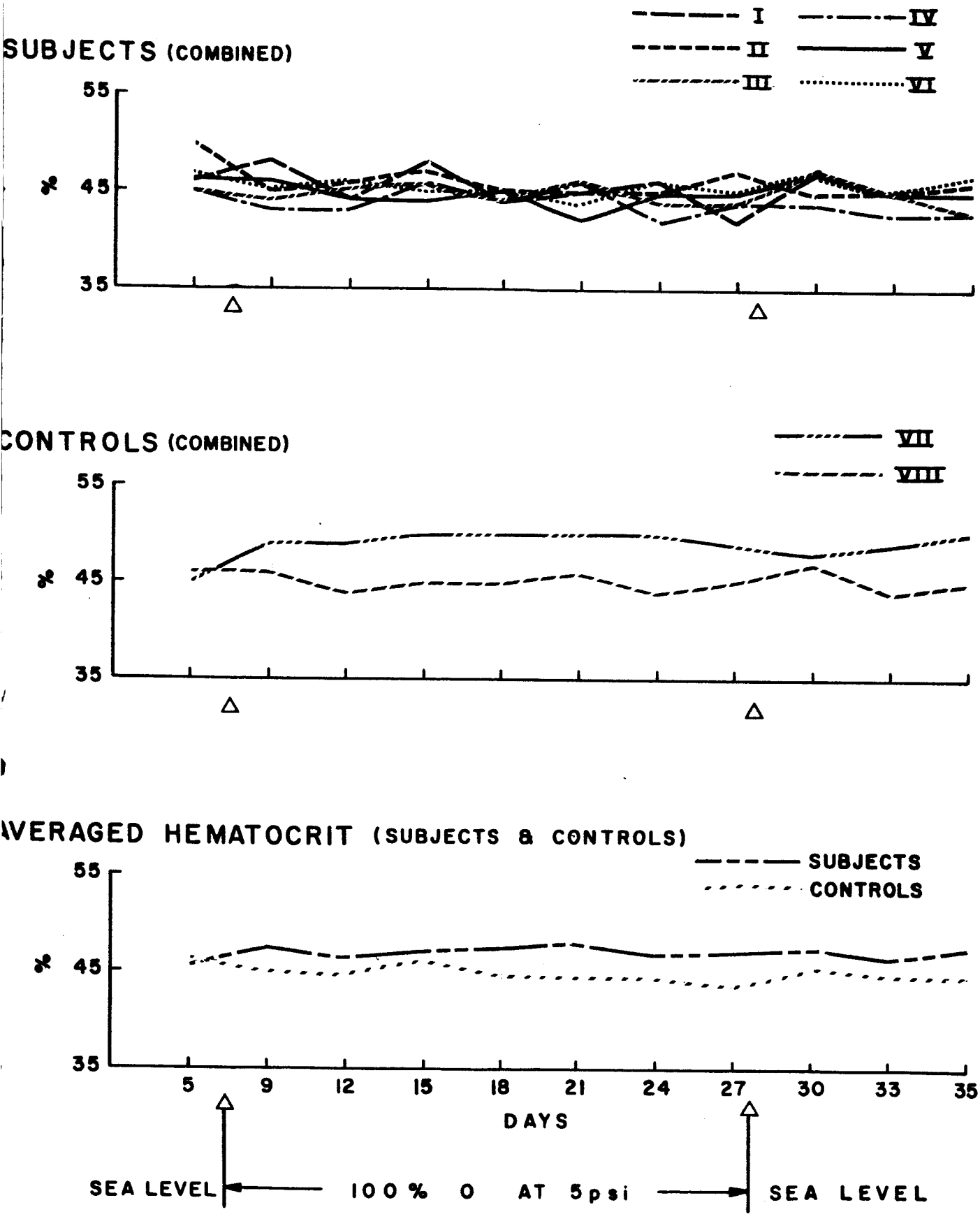


FIGURE 5-1. HEMATOCRIT

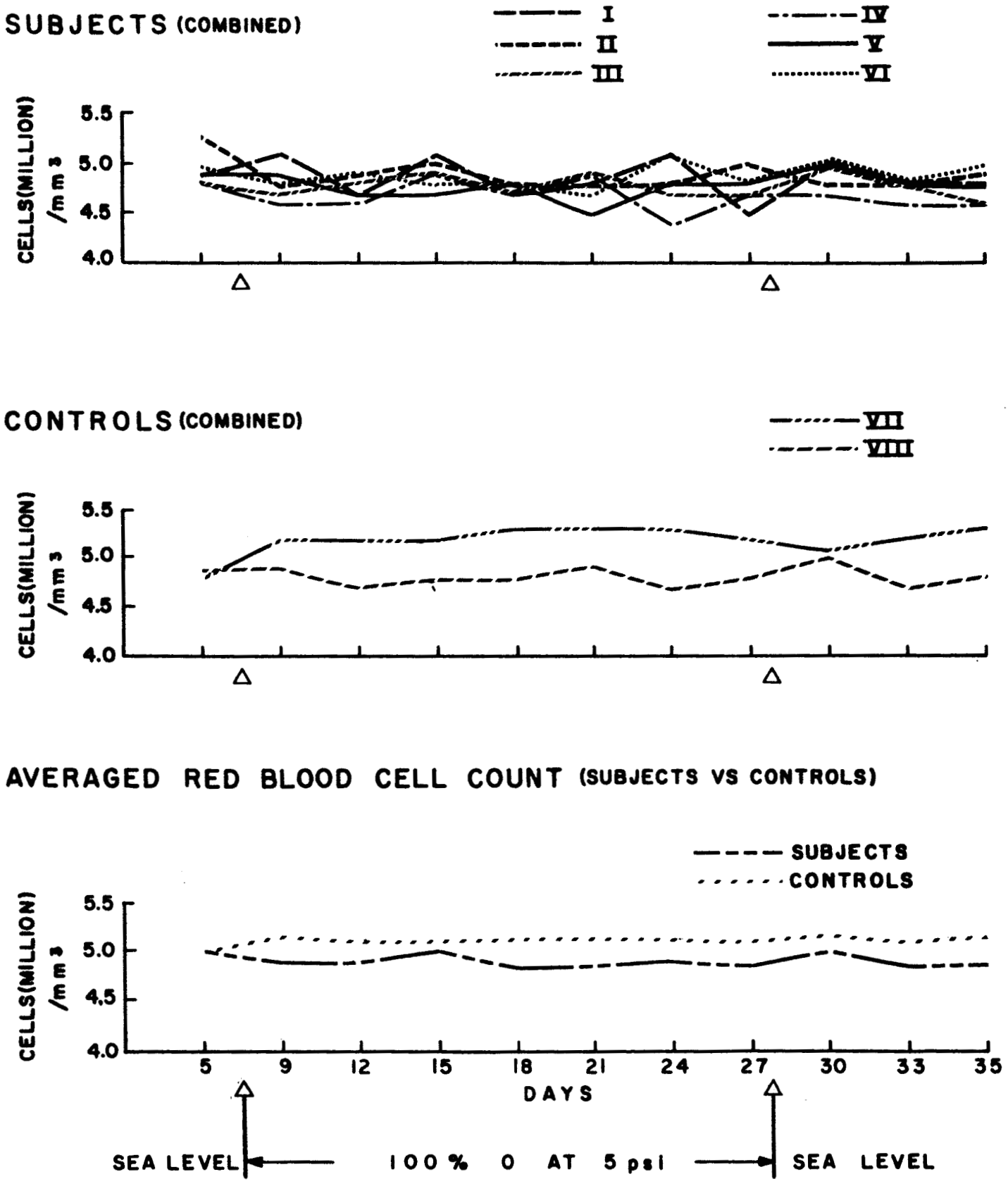


FIGURE 5-2 RED BLOOD CELL COUNT

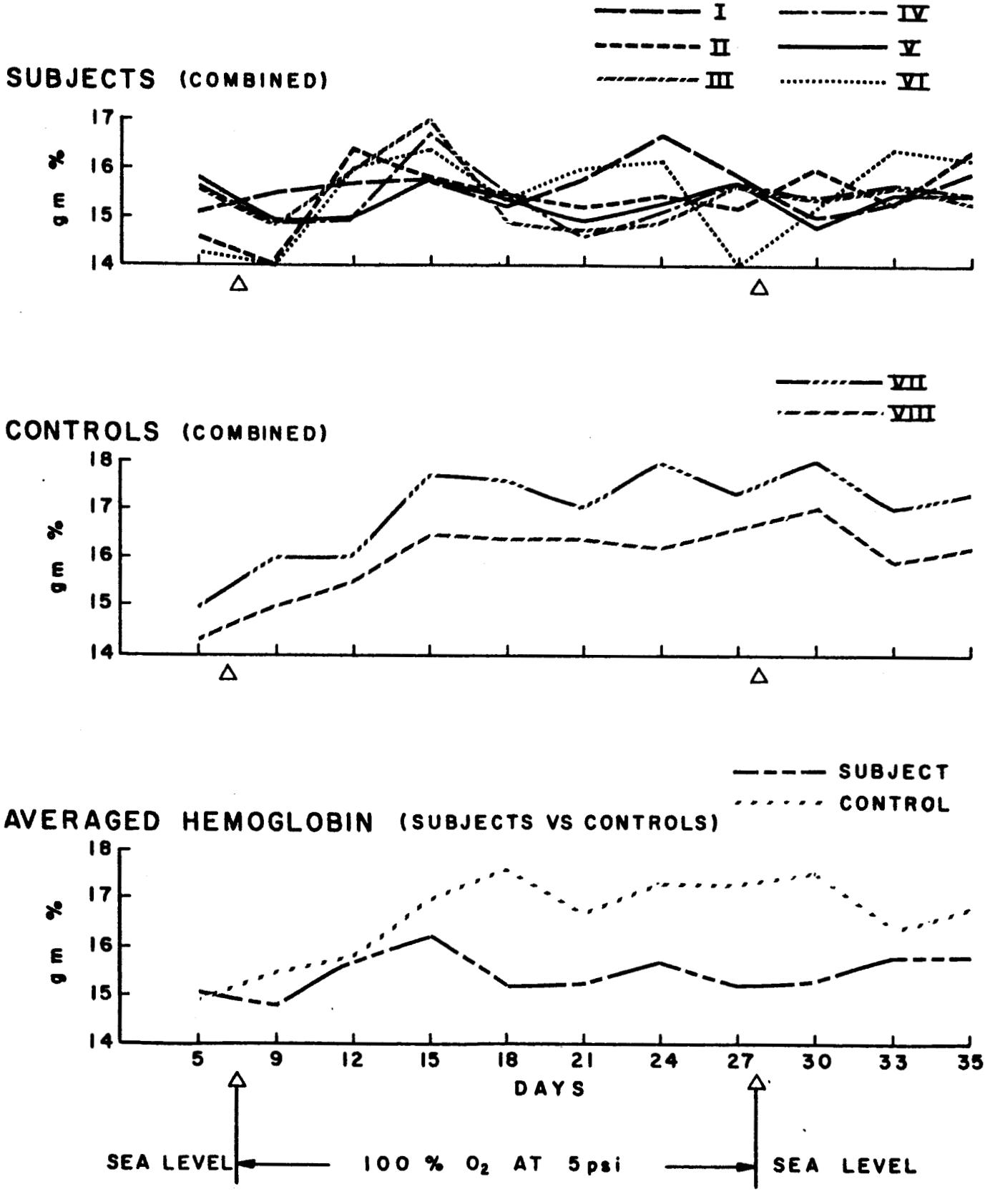
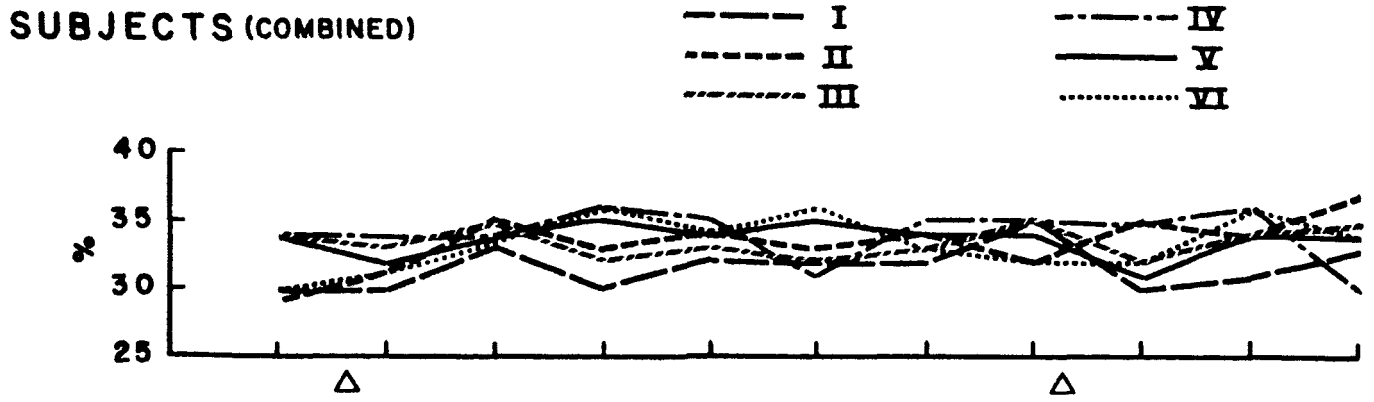
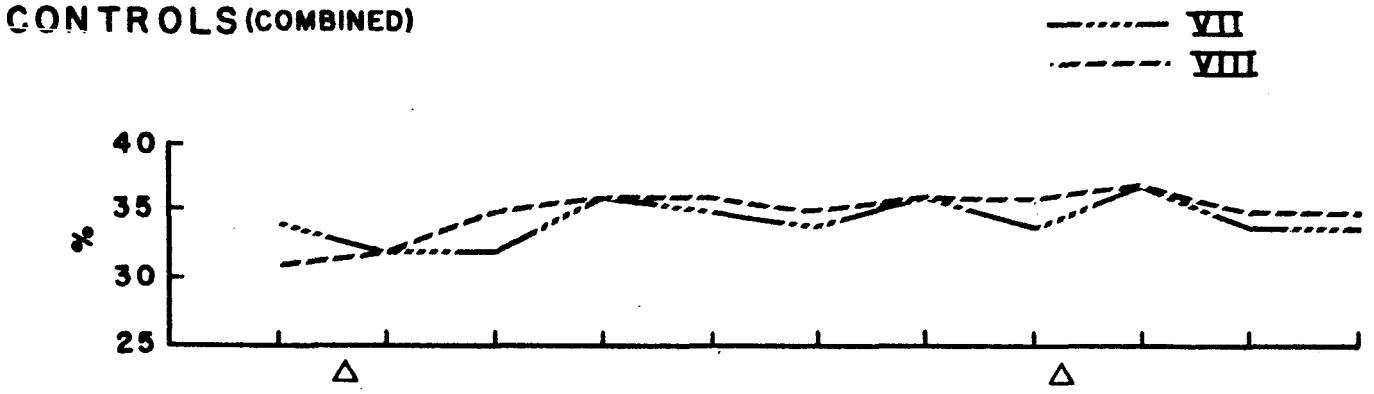


FIGURE 5-3. HEMOGLOBIN





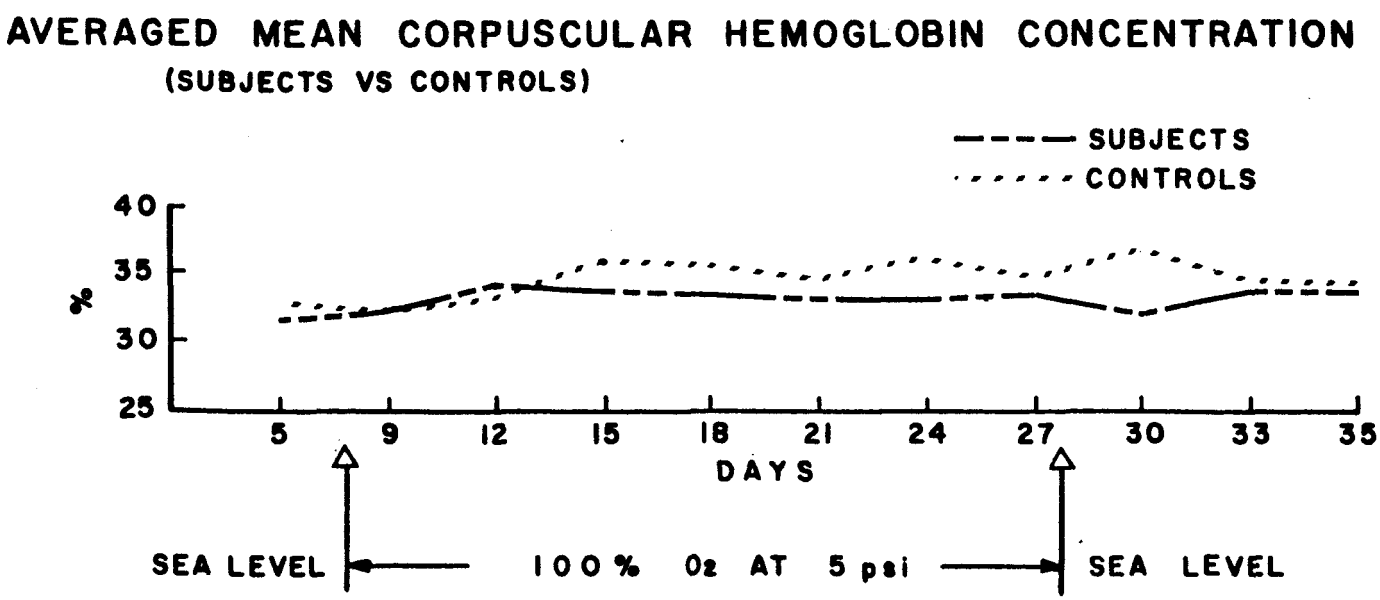


FIGURE 5-4. RED BLOOD CELL INDICES - MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION

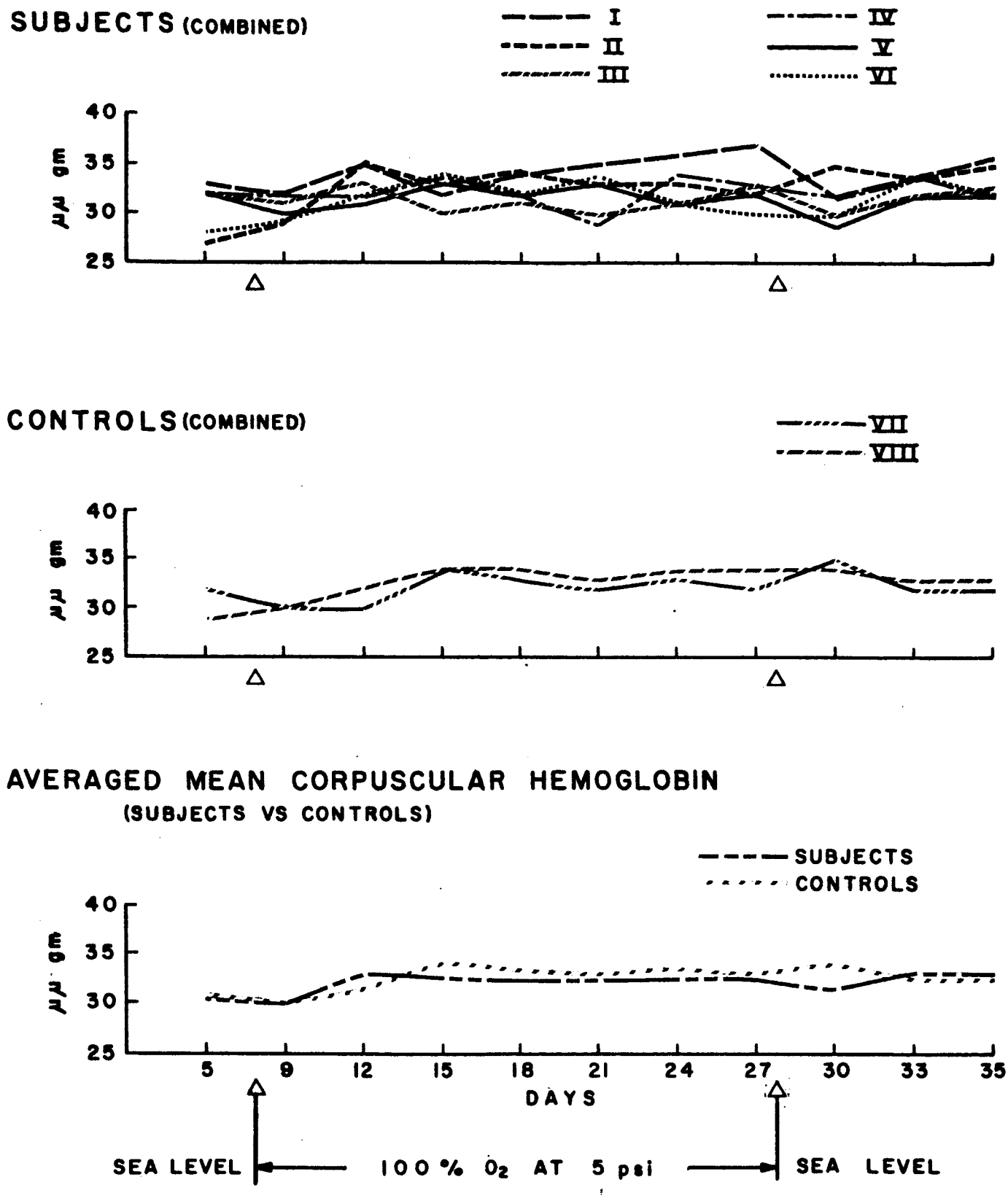


FIGURE 5-5. RED BLOOD INDICES - MEAN CORPUSCULAR HEMOGLOBIN

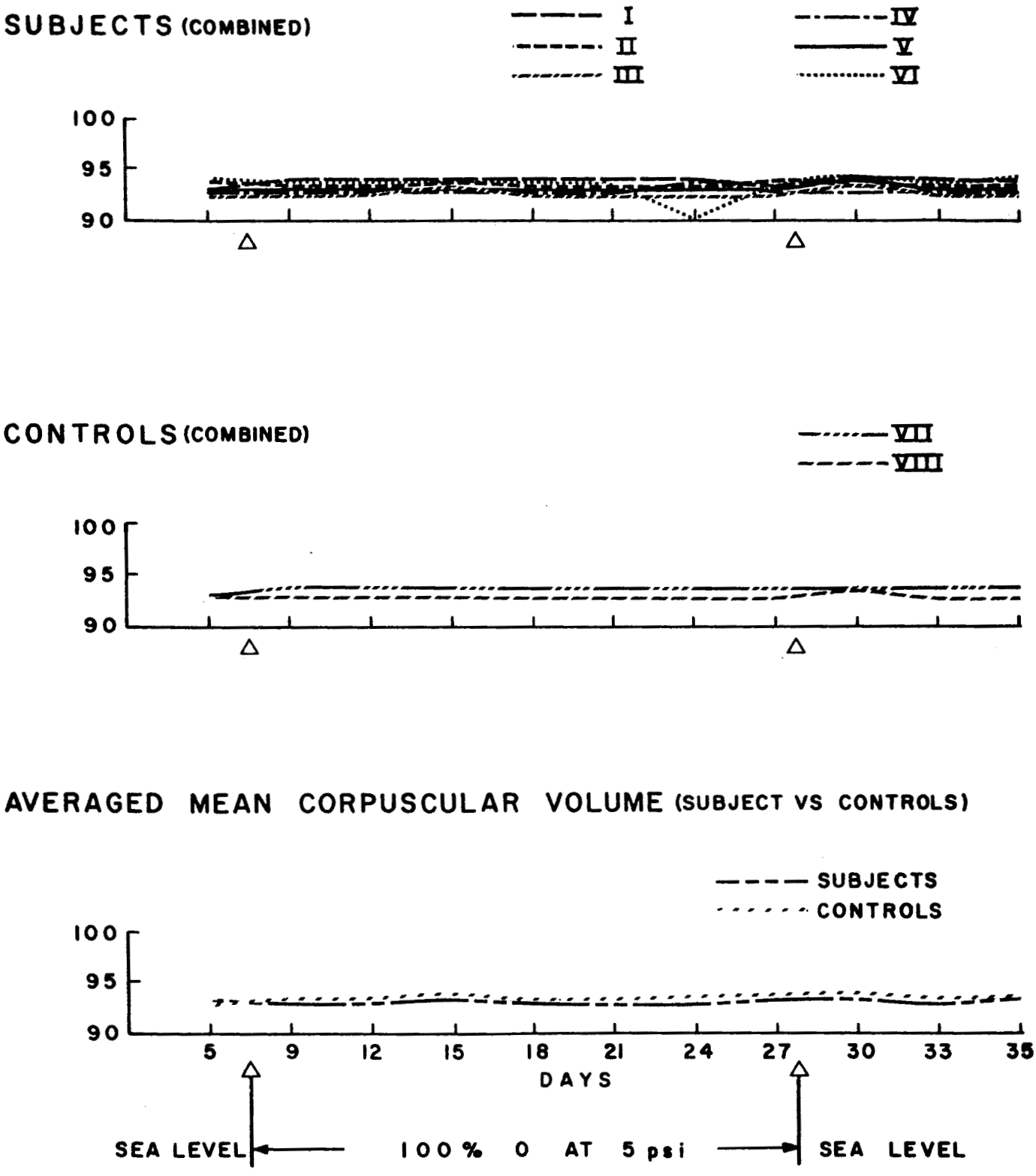


FIGURE 5-6. RED BLOOD INDICES - MEAN CORPUSCULAR VOLUME

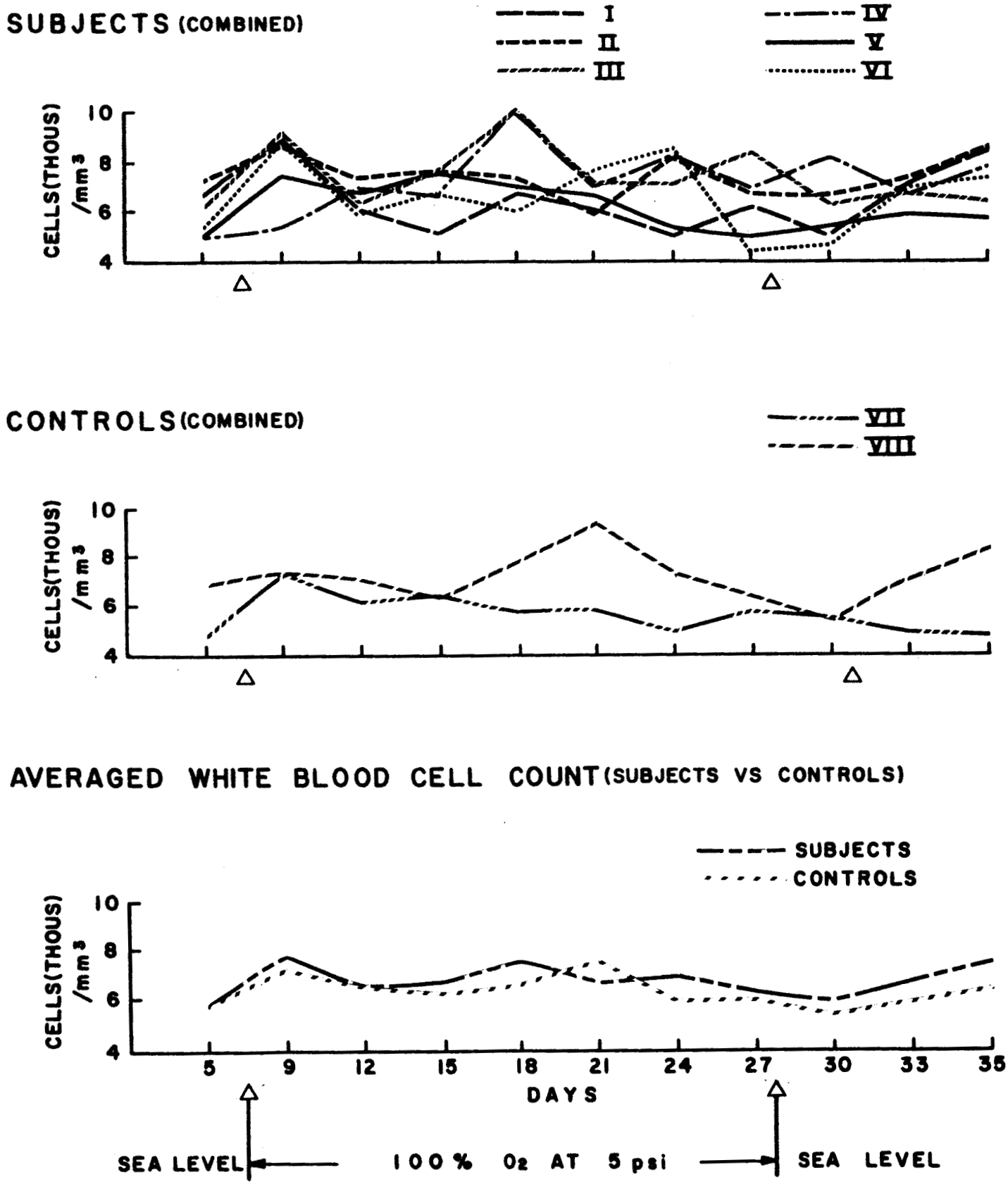


FIGURE 5-7. WHITE BLOOD CELL COUNT

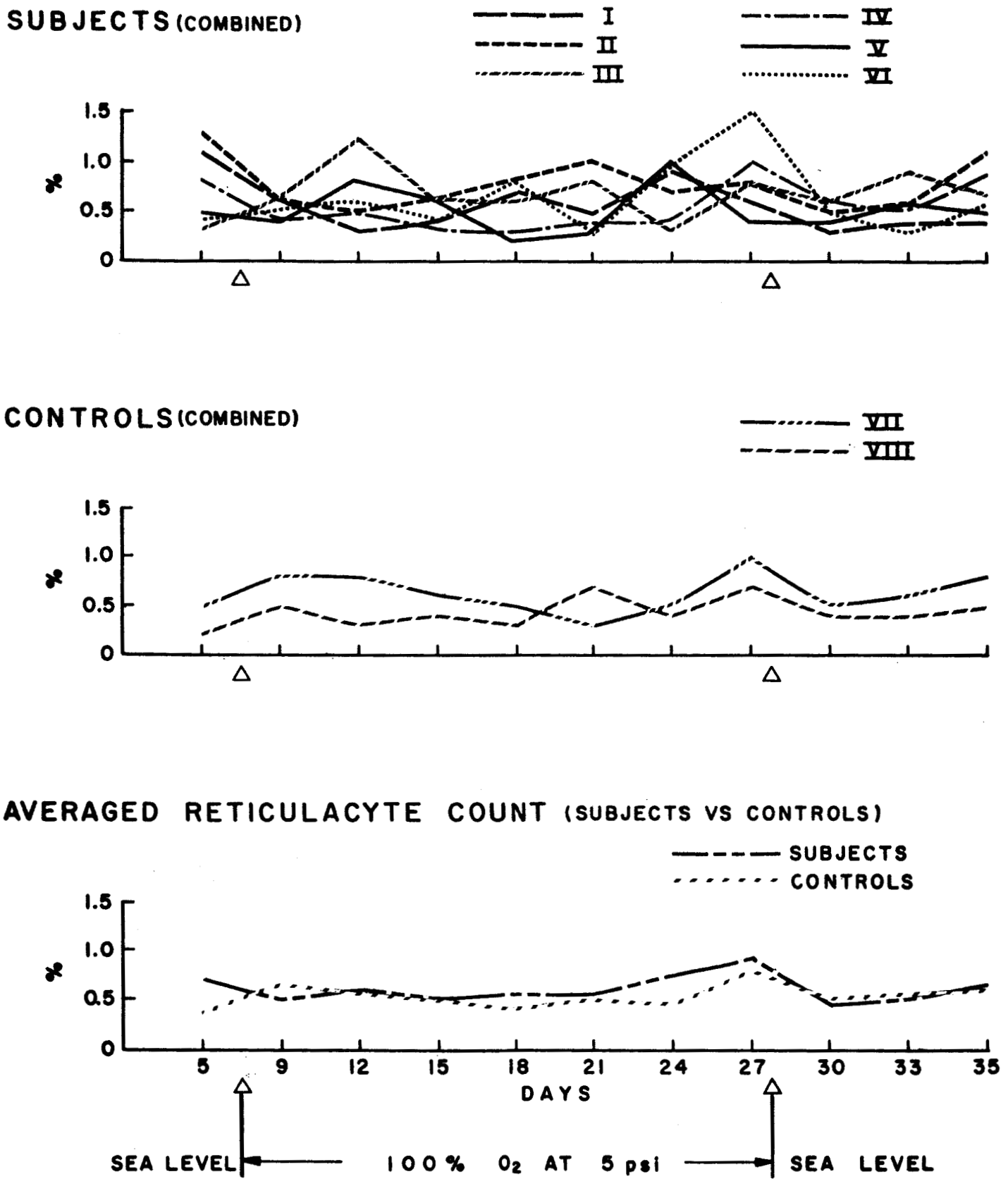


FIGURE 5-8. RETICULOCYTE COUNT

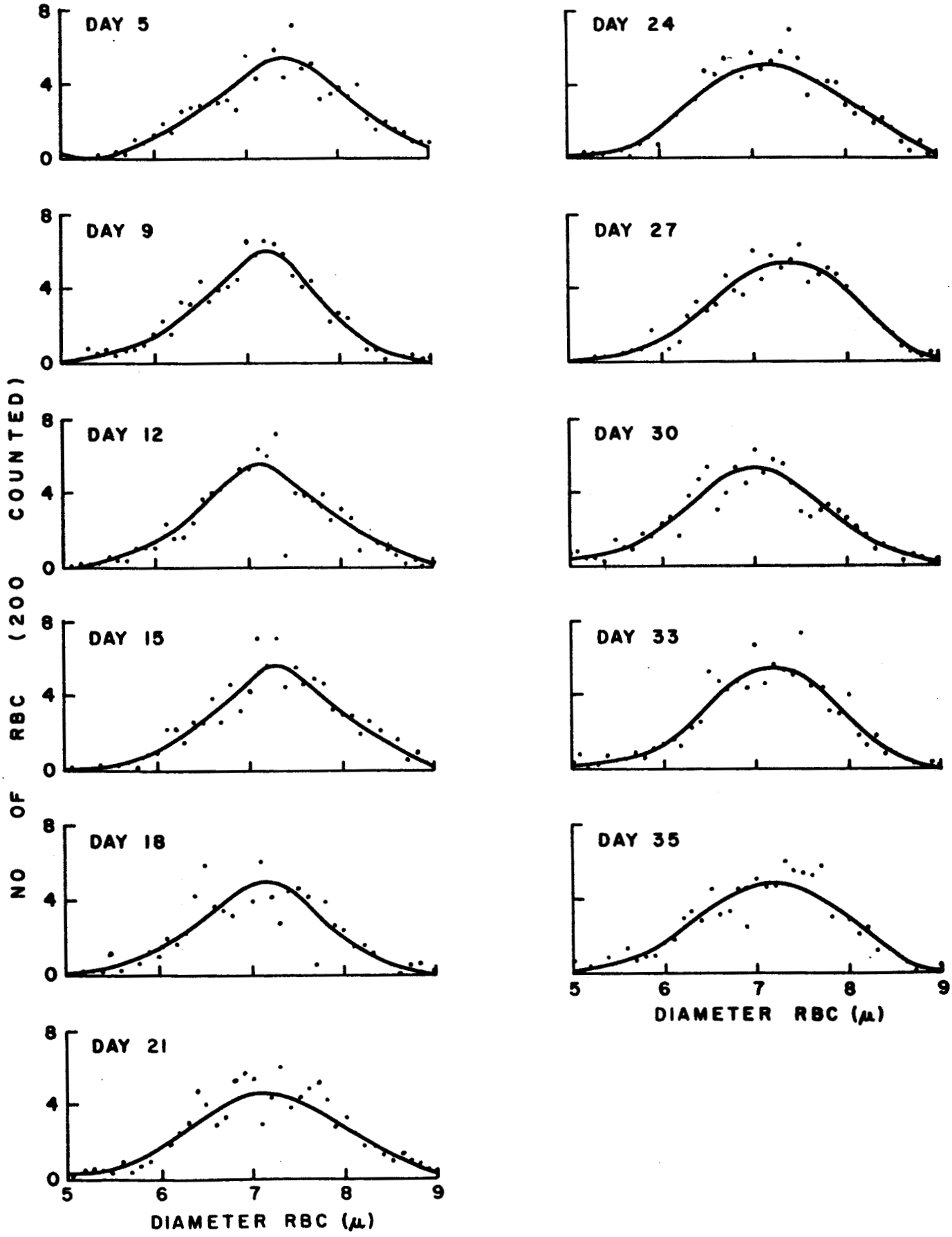


FIGURE 5-9. PRICE-JONES CURVE - SUBJECTS (AVERAGED)

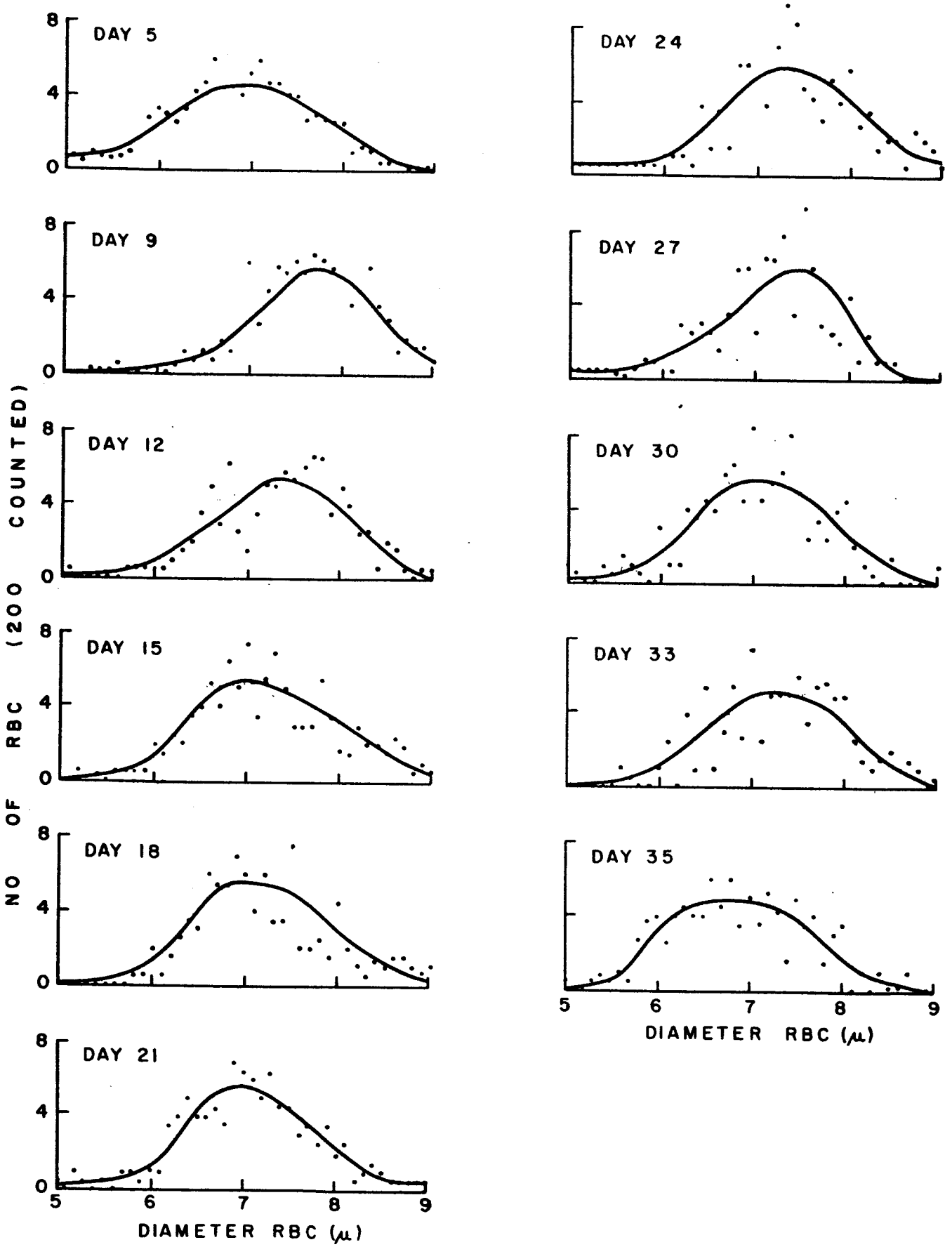


FIGURE 5-10. PRICE-JONES CURVE - CONTROLS (AVERAGED)

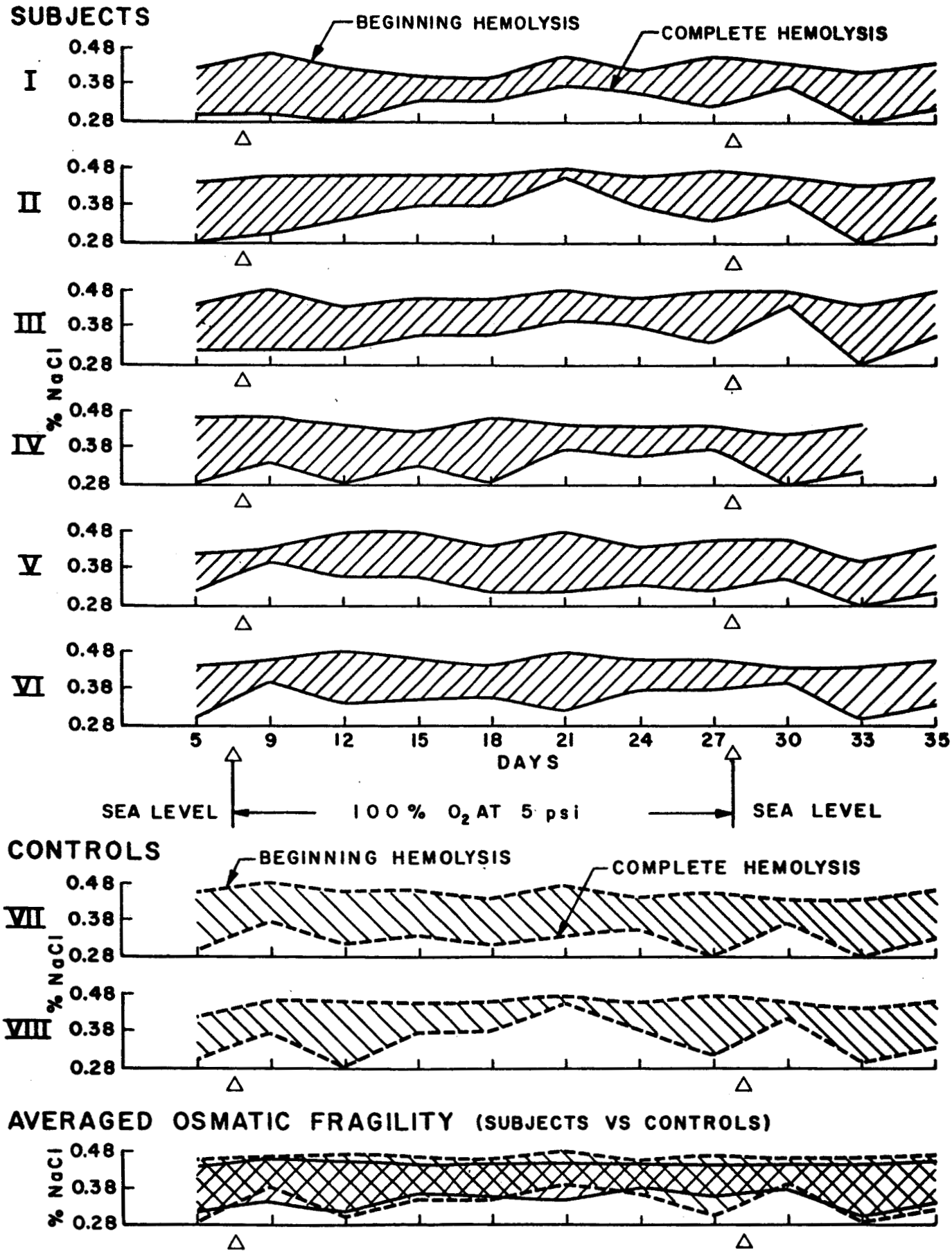


FIGURE 5-11. OSMOTIC FRAGILITY

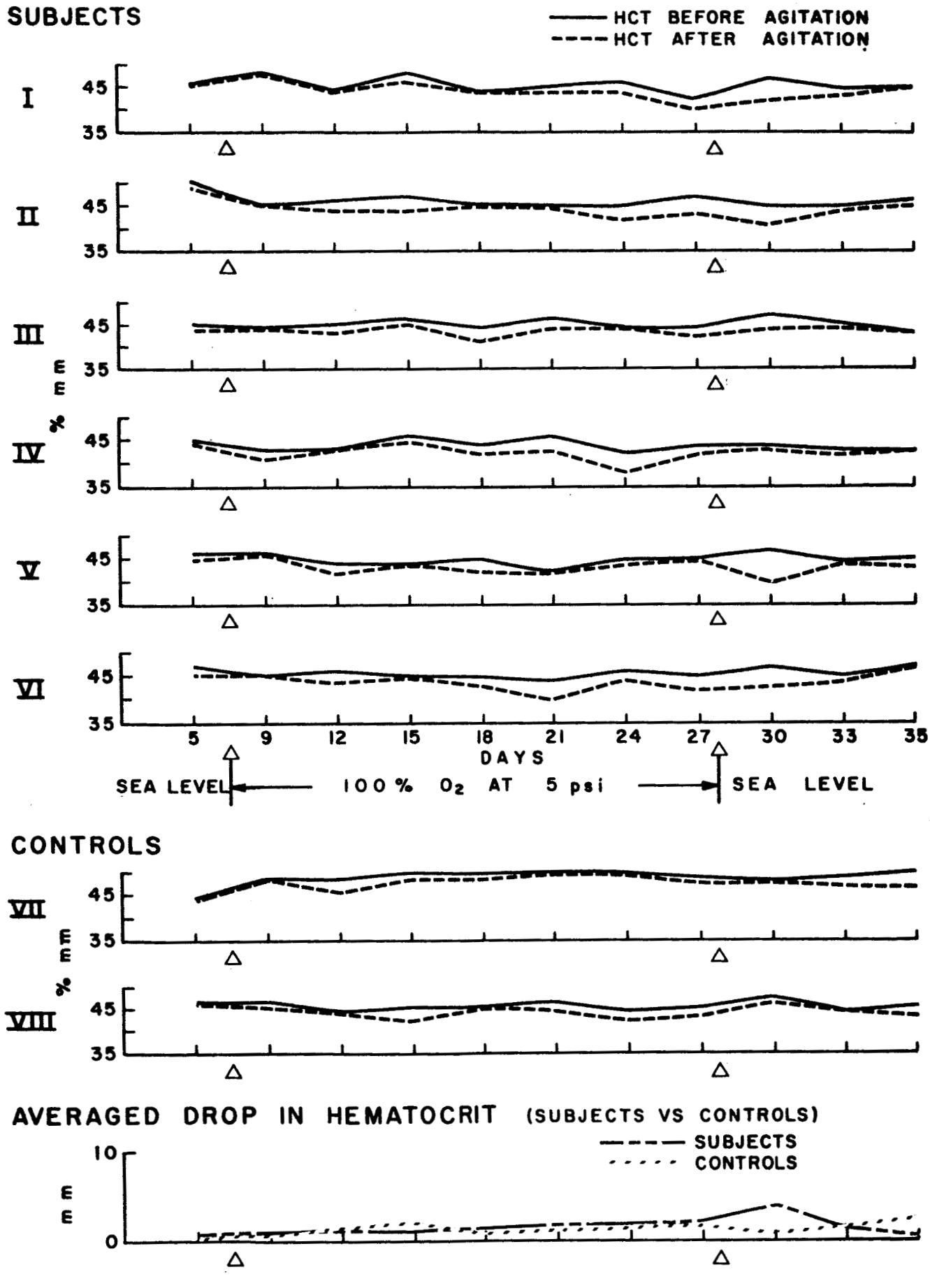
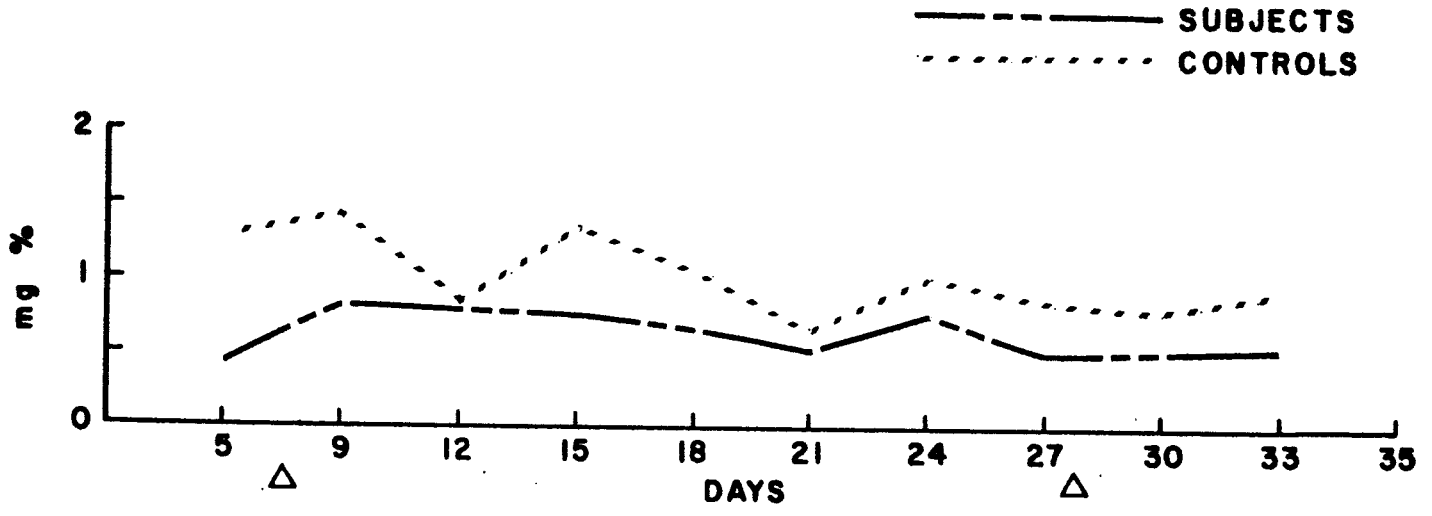
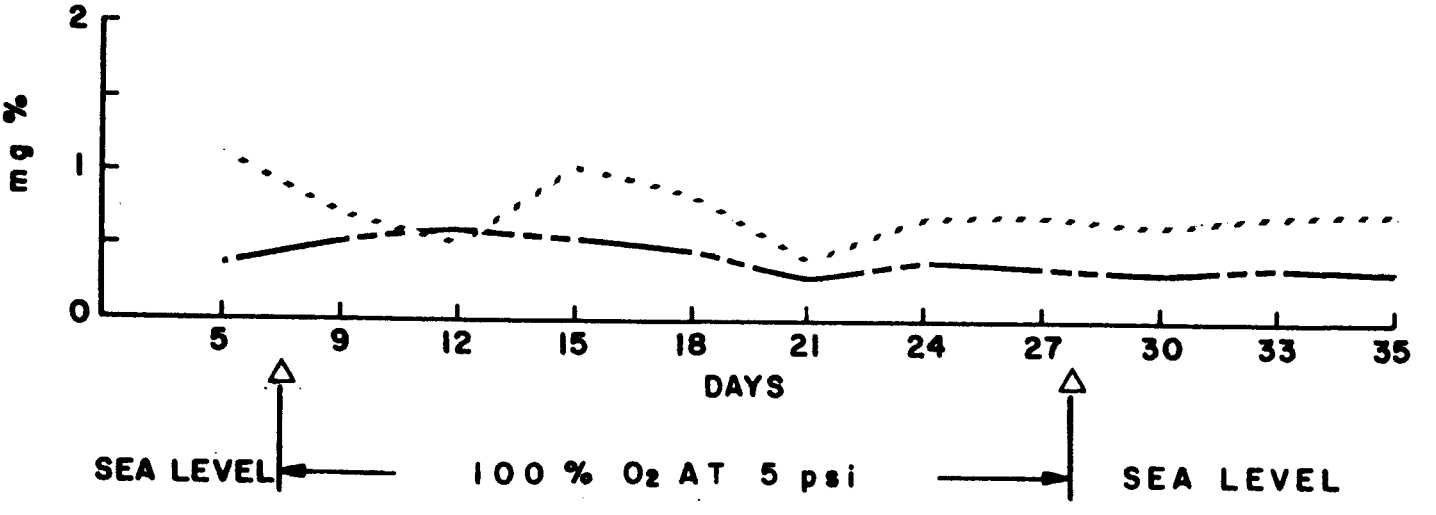


FIGURE 5-12. MECHANICAL FRAGILITY



AVERAGED TOTAL BILIRUBIN



AVERAGE INDIRECT BILIRUBIN

FIGURE 5-13.

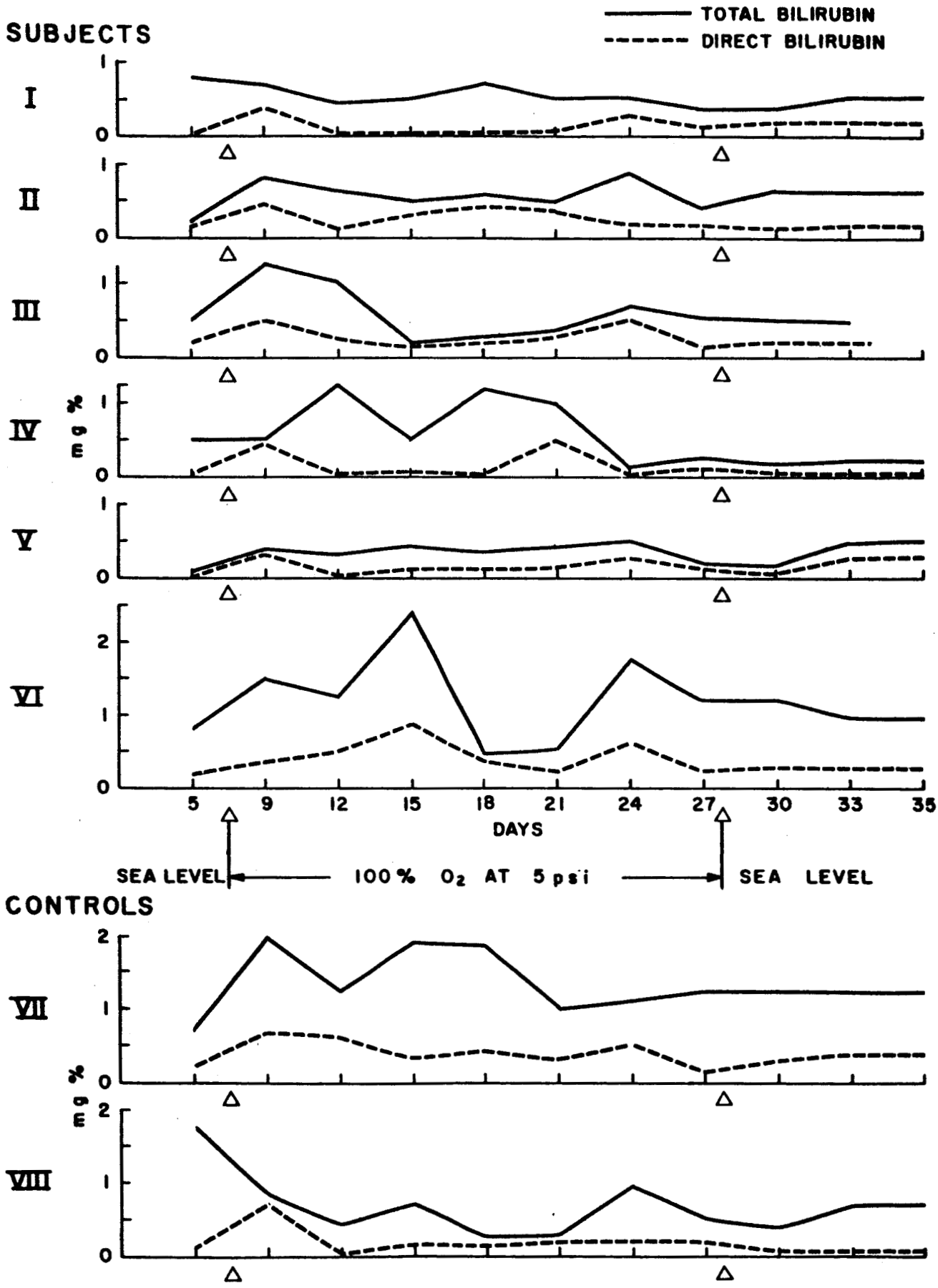


FIGURE 5-14. TOTAL AND DIRECT BILIRUBIN

SECTION 6

BIOCHEMICAL EFFECTS OF PROLONGED EXPOSURE TO AN ATMOSPHERE OF 100% OXYGEN AT A SIMULATED ALTITUDE OF 27,000 FEET

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SECTION 6

BIOCHEMICAL EFFECTS OF PROLONGED EXPOSURE TO AN ATMOSPHERE OF 100% OXYGEN AT A SIMULATED ALTITUDE OF 27,000 FEET

In the course of evaluating the proposed single gas system for spacecraft atmospheres, several reports have concerned themselves with the physiological effects of 100% oxygen atmosphere of these vehicles. In one of the early reports[1] several physiological effects of the system were noted on human volunteers. The most striking of these was an apparent tendency toward in vivo hemolysis. Within several hours of the time of entry a rise in circulating serum bilirubin was noted in the subjects with a corresponding loss of hemoglobin. It was concluded that there were toxic manifestations of the oxygen atmosphere and further study of the physiological and biochemical effects of the oxygen atmosphere was indicated.

In several other reports [2, 3, 4], various biochemical determinations were done on human subjects that were exposed to atmospheres containing increased oxygen partial pressures at reduced atmospheric pressure, but not necessarily 100% oxygen. Although the question of hemolysis was not specifically examined, no mention was made of any observations concerning it other than a slight drop in hematocrit which subsequently returned to pre-exposure levels[4]. There were no untoward effects described in the subjects.

In one recent study[5] particular consideration was directed to the possible hemolytic effects of atmospheres containing increased partial pressures of oxygen on human subjects. A slight drop in the hematocrit was observed ranging from 6.7% to 9.1%, but normal Cr^{51} red cell survival, normal bilirubin and urobilinogen excretion, and low reticulocyte counts led the authors to the conclusion that there was no hemolytic process active. They also investigated the pentose phosphate pathway in the red cell by measuring the activity of glucose-6-phosphate dehydrogenase activity and glutathione stability and found, by these criteria, that oxidative hemolysis was not occurring. This study was conducted in atmospheres that ranged from 33% to 98.5% oxygen.

There have been several indications that one of the potential hazards concerned with human survival in atmospheres of increased oxygen tension is the inactivation of certain enzymes[6]. It has been noted that the dehydrogenases are particularly susceptible to this type of toxic action.

Previous studies in this laboratory[7] have shown a definite increase in the activity of serum isocitrate dehydrogenase in several human subjects exposed to an atmosphere of 100% oxygen at varying atmospheric pressures for periods of time up to 72 hours. In view of this, it was deemed advisable to include the assay of serum isocitrate dehydrogenase activity in the current experiment.

In view of conflicting reports in the literature concerning the influence of increased oxygen tensions on the activity of glucose-6-phosphate dehydrogenase in the erythrocyte, the measurement of the activity of this enzyme in the red cell was included.

In one of the previously cited studies[1] one of the subjects who showed a definite hemolytic response to an atmosphere of pure oxygen was later diagnosed as having a thalassemia trait. For this reason, and in order to adequately screen our subjects before exposing them to the high oxygen atmosphere, electrophoretic analysis of their hemoglobin types was conducted.

Haptoglobin is an alpha-2 globulin which can combine with hemoglobin in the serum to form a weak peroxidase. When hemoglobin is liberated into the serum, as in hemolysis, it combines with haptoglobin until the binding capacity of the haptoglobin is exceeded. In hemolytic conditions, therefore, the plasma level of free haptoglobin is reduced. In order to further screen for possible hemolytic effects, electrophoretic analysis of serum hemoglobin binding capacity was carried out.

It was also noted in previous experiments in this laboratory that there appeared to be, in certain subjects, an increase in the lipoidal content of the serum as evidenced by a turbid, lactescent serum. It is known that there is virtually no "free" lipid material in the serum, but that most of it is bound to protein. In many types of lipemia it is more valuable to determine the distribution of the relative concentrations of the lipoprotein fractions than the total concentration of a specific lipid in the serum[8]. Lipoprotein electrophoresis was carried out on the sera of the subjects of this study.

METHODS

All subjects for this study were Navy and Marine Corps aviators who were between 25 and 28 years old. All were considered to be in excellent physical condition, having been drawn from a pool of potential astronaut candidates who had successfully met the exacting physical and psychological qualifications set down by the National Aeronautics and Space Administration for astronauts.

The subjects were confined in a low pressure chamber for a total of 34 days. During the first 7 days the chamber was maintained at ambient sea level conditions. On the 8th day, the chamber was pumped out to a simulated altitude of 27,000 feet and an atmosphere of 100% oxygen was introduced. These conditions were maintained for twenty days. On the 28th day, sea level conditions were restored to the chamber, but the subjects remained inside for an additional 7 days.

Two of the subjects, Numbers 3 and 6, served as controls and were maintained in an adjacent chamber under ambient conditions for the duration of the experiment. Except for the conditions of altitude and atmosphere, they were treated the same as the experimental subjects.

Isocitrate dehydrogenase activity was determined in the serum by a method based on that of Wolfson and Williams-Ashman[9] in which nicotinamide adenine dinucleotide phosphate (NADP) is incubated with isocitrate and manganese in a 1 centimeter long cell in a Beckman DU spectrophotometer. Following the addition of an aliquot of serum containing the enzyme, the increase in optical density caused by the generation of the reduced form of the co-enzyme is measured at a wavelength of 340 millimicrons and plotted against time. The conversion of one millimole of NADP to NADPH is caused by the oxidation of one millimole of substrate by the enzyme and the subsequent transfer of the hydrogen to the coenzyme. One "unit" of enzyme activity is the oxidation of one millimicromole of substrate per hour per milliliter of serum.

Glucose-6-phosphate activity was determined in a similar fashion by a method based on that of Kornberg and Horecker[10] in which the erythrocytes are washed several times with physiological saline in order to insure that any activity measured comes from the enzyme in the red cell and not in the plasma. The washed cells are then hemolyzed and incubated with NADP at a pH of 7.6 and the rate of appearance of NADPH is followed at 340 mu in a spectrophotometer following the addition of glucose-6-phosphate substrate. Activity of the enzyme is reported as micromoles of substrate oxidized per minute per gram of hemoglobin.

Hemoglobin electrophoresis was carried out in an acrylamide gel medium and the results were quantitated using a densitometer with a 500 mu interference filter, and compared with known standard types.

Haptoglobin levels were also determined by an electrophoretic technique using an acrylamide gel medium. In this technique, hemoglobin in a known quantity is added to unhemolyzed serum and, following electrophoretic separation, the gels are scanned in a recording densitometer using a 500 mu interference filter. The unbound hemoglobin migrated ahead of the hemoglobin-haptoglobin complex. Any reduction in the free hemoglobin level is due to binding by the serum haptoglobins. A standard is run for comparison and the free hemoglobin in the unknowns is compared with the standard. The resulting amount of hemoglobin (in milligrams) bound by the haptoglobin is then calculated.

Lipoprotein electrophoresis was carried out on paper strips in a Durrum type cell. Following separation of the lipoprotein into the fractions that migrate with the alpha and beta globulin fractions, the strips are strained with oil red O and are scanned in a recording densitometer.

RESULTS

The results of the hemoglobin electrophoresis on the eight subjects used in the study are shown in Table 6-1. It can be seen that all are quite similar and do not demonstrate any high concentrations of hemoglobin type A_2. In normal subjects, type A_2 may be as high as 4.9 percent so these normal levels would indicate the absence of a thalassemia trait in any of the subjects. Alkali denaturation tests showed that there was no type F in any of the subjects.

Serum isocitrate dehydrogenase activities are shown in Table 6-2. Although there are slight variations in the day to day activities in several of the subjects, there is no consistent trend. For these determinations as well as for the glucose-6-phosphate dehydrogenase determinations, specimens drawn during the 5th and 7th days that the subjects were in the chamber are used as baselines, since during this time the atmosphere of the chamber was ambient air at sea level pressure. Subjects No. 3 and 6 were the "controls" who were isolated during the same period of time, but were not exposed to any conditions of altitude or changes in atmosphere.

The activities of glucose-6-phosphate dehydrogenase in the erythrocytes are shown in Table 6-3. Hemolysates were made of red cells that had been drawn with heparin as anticoagulant and washed three times with physiological saline. The hemoglobin content of the hemolysate was determined and enzyme activity related to this rather than to a volume of blood in order to eliminate erroneous results that could arise from cells being lost during the washing procedure.

The results of the electrophoretic determination of serum haptoblobin levels are presented in Table 6-4. Care was taken to insure that the sera analyzed were clear and unhemolyzed in order to eliminate spurious results that could arise from mechanical hemolysis.

The distribution of the serum lipoproteins between the fractions that migrate electrophoretically with the alpha and beta globulins are presented in Table 6-5.

DISCUSSION

The values for the serum isocitrate dehydrogenase are all constant and show no elevation or depression. It must be emphasized that subject selection was different in this experiment than in the ones that have previously been done in this laboratory. In the first series of experiments, the elevations that occurred were in two subjects that were in their late thirties, and were not considered to be in extremely good physical condition. The subjects for this study were all young pilots and in excellent physical condition. In earlier work in this field, subjects for the most part were of a relatively young age.

Glucose-6-phosphate dehydrogenase activity also remained constant in the erythrocytes of the subjects. This agrees with previous studies in this laboratory as well as those of another group[5]. There appears to be no type of oxidative hemolysis occurring in our subjects. Therefore, the hemolysis which has been reported by others still remains unexplained.

All of the subjects included in this study had normal hemoglobin types. It would seem advisable however, in view of a literature report of a hemolytic episode that occurred in one subject exposed to a pure oxygen atmosphere[1] who had an abnormal hemoglobin, the identification of hemoglobin types be carried out in all subjects to be exposed to atmospheres of this type.

The levels of serum haptoglobin appear to remain relatively constant throughout the course of the experiment based on hemoglobin binding capacity, There is some variation in the day to day levels, but it is felt that these are within the limits of the method. At any rate, there is no definite increase in the amount of circulating haptoglobin-bound hemoglobin which is evidence that there was no hemolysis occurring.

There is also some variation in the day to day levels of the serum lipoprotein electrophoretic fractions. These are well within the limits of the method and do not show any trend that would be indicative of an interference with lipid metabolism. In the previous studies in this laboratory the subjects were not considered to be in as good physical condition as the subjects used in this study. There were also several cases of dysbarism in the subjects used in the previous study which accounted for some degree of emotional stress in the other subjects. In contrast, there was no apparent degree of stress or apprehension on the part of the subjects used in the current study. It has been observed many times in the past that emotional stress can account for the appearance of varying degrees of lipid material in the circulating blood as the stores of depot lipid are mobilized and transported.

SUMMARY AND CONCLUSIONS

Six human subjects were exposed to an atmosphere of 100% oxygen for a period of 20 days at a simulated altitude of 27,000 feet in the low-pressure chamber of the Aerospace Crew Equipment Laboratory, Naval Air Engineering Center, Philadelphia, Pa. Two subjects were subjected to the same regimen, in an adjacent chamber with the exception that they remained in an atmosphere of ambient, sea-level air, and served as controls.

There was no evidence obtained from biochemical data to suggest that a 100% oxygen atmosphere at a simulated altitude of 27,000 feet is injurious to otherwise healthy subjects.

The activities of serum isocitrate dehydrogenase, and erythrocytic glucose-6-phosphate dehydrogenase remained constant throughout the period of exposure and did not deviate from baseline or control levels.

Similarily, there was no deviation from baseline or control levels of serum haptoglobin as evidenced by the ability of that serum protein to bind hemoglobin or in the relative distribution of serum lipoproteins between the alpha and beta fractions.

ACKNOWLEDGMENTS

The electrophoretic analyses reported in this paper were performed by LCDR T. G. Ferris, MSC, USNR, Officer in Charge, Rear Admiral Calver's Physical Chemistry Laboratory, Naval Medical School, National Naval Medical Center, Bethesda, Maryland, 20014.

Many of the enzyme analyses and much of the monitoring of the experiment were done by HMC B. G. Kester, USN.

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TABLE 6-1

Hemoglobin Types

Subject No.		Hgb. Type A	Hgb. Type A_2
1		95.9%	4.1%
2		98.5%	1.5%
3	(control)	97.0%	3.0%
4		98.5%	1.5%
5		96.3%	3.7%
6	(control)	97.5%	2.5%
7		99.6%	0.4%
8		97.8%	2.2%

TABLE 6-2

Serum Isocitrate Dehydrogenase Activity
(Millimicromoles of substrate oxidized per hour per milliliter of serum)

		Day in chamber										
Subject Number		5*	7*	9	12	15	18	21	24	27	30	35
1		44	58	52	52	41	46	52	46	58	45	45
2		89	116	104	52	81	70	99	87	81	104	88
3	(control)	78	52	58	46	47	N.S.	52	46	65	64	58
4		87	81	81	102	64	58	81	87	64	99	58
5		58	76	81	58	70	70	75	75	58	75	70
6	(control)	51	76	70	52	46	59	70	87	87	70	52
7		88	87	99	76	52	52	70	99	104	99	64
8		73	58	80	46	73	41	64	87	87	70	64

* Baseline values

TABLE 6-3

Erythrocyte Glucose-6-Phosphate Dehydrogenase Activity
(micromoles of substrate oxidized per minute per gram of hemoglobin)

	Day in Chamber											
Subject Number	5*	7*	9	12	15	18	21	24	27	30	33	35
1	3.6	3.2	3.8	3.4	4.1	5.4	4.2	5.8	5.3	4.2	3.3	4.5
2	4.6	4.5	5.5	3.3	5.0	5.7	5.6	5.4	6.4	5.1	4.7	5.0
3 (control)	3.6	3.6	3.9	3.0	4.7	4.6	3.4	4.0	3.3	4.2	3.6	4.0
4	3.7	3.0	3.8	4.4	3.9	4.5	2.7	4.8	5.2	4.7	4.7	4.4
5	4.1	3.7	4.0	4.4	4.4	4.0	3.5	4.7	5.4	4.3	5.4	4.2
6 (control)	4.2	3.9	4.0	4.4	4.0	5.4	4.4	4.2	5.5	5.2	3.2	4.5
7	3.9	3.6	4.4	5.2	4.8	4.2	3.8	4.1	5.5	4.4	4.7	4.7
8	4.1	3.8	4.4	3.5	4.3	4.5	4.5	4.8	5.3	4.6	4.2	4.9

* Baseline values

TABLE 6-4

Serum Hemoglobin Binding Capacity
(Milligrams of hemoglobin bound by serum haptoglobin)

	Day in chamber								
Subject Number	9*	12*	18	21	24	27	30	33	35
1	223	178	223	NS	225	179	183	256	308
2	NS	151	215	246	196	185	209	202	177
3 (control)	132	261	292	231	174	NS	222	162	236
4	193	NS	246	238	218	296	300	243	272
5	NS	NS	269	308	196	NS	208	196	207
6 (control)	NS	NS	269	193	131	156	208	217	183
7	NS	NS	292	269	189	185	202	182	207
8	182	172	162	246	182	193	234	189	248

* -Baseline values

NS-No specimen

TABLE 6-5

Serum Lipoprotein Fractions
(Percent distribution)

Subject Number		Day in chamber									
		5*	9*	12	18	21	24	27	30	33	35
1	Alpha	11.9	18.9	12.6	23.5	21.1	14.5	19.1	11.9	13.6	13.2
	Beta	88.1	81.1	87.4	76.5	78.9	85.5	80.0	88.1	86.4	86.8
2	Alpha	8.0	NS	6.8	23.9	20.0	16.0	15.0	5.4	16.5	12.3
	Beta	92.0		93.2	76.1	80.0	84.0	85.0	94.6	83.5	87.7
3	Alpha	7.7	15.3	8.1	21.4	18.0	12.0	13.2	9.7	16.8	13.2
	Beta	92.3	84.7	91.9	78.6	82.0	88.0	86.8	90.3	83.2	86.8
4	Alpha	6.6	9.5	5.1	14.8	6.5	8.0	8.0	5.2	5.9	9.3
	Beta	93.4	90.5	94.9	85.2	93.5	92.0	92.0	94.8	94.1	90.7
5	Alpha	11.0	17.3	10.9	16.0	18.4	13.0	13.0	12.8	11.3	13.3
	Beta	89.0	82.7	89.1	84.0	81.6	86.1	87.0	87.2	88.7	86.7
6	Alpha	9.4	17.4	13.8	22.4	20.0	12.8	16.0	10.3	9.8	13.0
	Beta	90.6	82.6	86.2	77.6	80.0	87.2	84.0	89.7	90.2	87.0
7	Alpha	6.1	20.8	4.4	32.6	20.6	NS	23.8	15.6	19.5	27.5
	Beta	93.9	79.2	95.6	67.4	79.4		76.2	84.4	80.5	72.5
8	Alpha	14.3	11.0	15.4	22.0	22.7	16.4	12.6	12.0	13.8	15.7
	Beta	85.7	89.0	84.6	78.0	77.3	83.6	87.4	88.0	86.2	84.3

* -Baseline values

NS-No specimen

SECTION 7

PULMONARY FUNCTION AND X-RAY

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SECTION 7

PULMONARY FUNCTION AND X-RAY

The response of the respiratory system to the internal environment of manned spacecraft has been of interest to many investigators. The use of 100% oxygen at reduced pressures has prompted concern over the possibility of producing alterations in the normal patterns associated with pulmonary function. [1-11] Although a recent study involving 14 subjects at 258mmHg. on 100 percent oxygen produced no demonstrable changes in pulmonary function, it was decided to extend the period of exposure and to test the validity of previously collected data.

Tests and Methods

The following tests and measurements were performed: tidal volume (TV), expiratory reserve volume (ERV), inspiratory capacity (IC), vital capacity (VC), functional residual capacity (FRC) and carbon monoxide diffusing capacity (D_{CO}). In addition, base line data was obtained for arterial P_{O2}, P_{CO_2}, and $_pH$ so that a more complete work up could be accomplished if any clinical signs, symptoms, or other measurements indicated a need.

The subjects were trained to perform the tests and record the data. Lung volumes were determined using a standard 13.5 liter Collins Respirometer. D_{CO} was determined by the single breath technique [13, 14]. The alveolar volume during breath holding was determined by adding the inspired volume to the residual volume. The inspired volume was read from the spirometer record and the residual volume calculated by body plethysmography prior to confinement. The time of breath holding was taken from the start of inspiration to the start of alveolar sample collection.

Prior to confinement each subject breathed 100% oxygen at sea level for thirty minutes or more before arterial samples were drawn from the anesthetized femoral artery into a heparinized, 10 cc syringe. The sample was then immediately introduced into the blood gas analysis apparatus (Instrumentation Laboratory Model 5113) which was located only a few feet from the subject. The apparatus was calibrated with both tonometered blood and wet gases. The calibration was again checked immediately preceding the introduction of each new sample.

TV, ERV, IC, VC determinations were made daily throughout the entire test profile, always in the morning before eating. FRC determinations were made during the week prior to confinement. The subjects were taken to the University of Pennsylvania where Dr. Arthur DuBois determined FRC and Dr. Gordon Powers familiarized the subjects with the single breath D_{CO} instrumentation and techniques. This equipment was then borrowed and set up in the altitude chamber at Aerospace Crew Equipment Laboratory (ACEL) and the subjects trained. A total of nine D_{CO} determinations were made on each test subject and six on each of the controls. Gas analysis and data reduction were completed at the University of Pennsylvania by Dr. Powers. The measurements were made prior to and following the altitude-100% oxygen environment exposure.

The FRC determinations were repeated five times on each of the subjects prior to the start of the run. These data are presented in Table 7-3. As there were no changes noted in other pulmonary function tests made during and after the altitude phase no follow up measurements were made. These data were collected solely as baseline data against which any observed change in pulmonary function could be compared. No such changes occurred.

Results

Tables 7-1 and 7-2 summarize the lung volume data for individuals and the group respectively. The tidal volumes appear high, however, these are not resting values. The subjects were engaged in routine activities of food preparation and body hygiene just prior to pulmonary function determinations. Beginning on the 22nd day of confinement subject #2 began to have abnormally high lung volumes which we subsequently determined to be erroneous due to technique. However, this could not be done until completion of the confinement period. Consequently the data on this subject from the 22nd day to the completion of the test profile were discarded and 3 determinations were made after confinement to complete the table. There appears to be a slight loss in vital capacity, approximately 150 cc, at altitude. This loss is so slight that if it were due to an anatomic or functional change it would be extremely difficult, if not impossible, to verify with present techniques and instrumentation.

Table 7-4 shows the D_{CO} values. In general the D_{CO} values are high normal and the variation is within the limits of experimental error especially since the tests were performed by the subjects on each other with relatively little training. No difference between pre-and post-altitude values are evident. The area and properties of the lung membrane and capillaries effecting gas exchange within the pulmonary alveoli did not measurably change as a result of the test profile or if any changes did occur they were rapidly reversible.

Table 7-5 presents the baseline data, collected for the same reason as the FRC, concerning arterial pH, P_{O_2} and P_{CO_2}.

The chest x-rays were obtained in the posterior-anterior and lateral projections two weeks prior to the study and on the twenty-sixth experimental day, that is, after the subjects had been at altitude breathing 100% oxygen for 19 days. X-ray films at altitude were made using a 200 ma., 100 kvp x-ray unit shooting through a 3.2 mm thick aluminum port in the outer chamber wall and through the inner chamber wall of 4.8 mm thick aluminum. The method for taking x-rays through the chamber walls is described in more detail in a previous report.[12]

Roentgenograms were interpreted by the Radiology Department of the U. S. Naval Hospital, Philadelphia. Chest x-rays obtained on the twenty-sixth experimental day showed no change from those taken two weeks prior to the study. Subject 5 had a small harmless osteoma on the left sixth rib which remained unchanged.

Discussion

Aside from the very slight drop in vital capacities there were no changes noted and, as the x-rays showed no evidence of atelectasis, the arterial punctures and FRC determinations were not repeated following the run.

It is possible that vital capacity measurements or chest x-rays may not be sensitive enough to detect small degrees of atelectasis. However, arterial oxygen tension as a measure of right to left shunt could also be insensitive as a measure of atelectasis because blood may cease to flow through the collapsed regions.

Conclusions

It would appear that healthy young men show no significant alterations in pulmonary function as a result of exposure to 100 percent oxygen at a pressure of 258 mmHg for 20 days.

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TABLE 7-1

Mean lung volumes Liters BTPS for individual test and control subjects

Subject		TV	ERV	IC	VC
1	A	930	2420	3700	6280
	B	800	2570	3530	6140
	C	800	2020	3840	6110
	D	980	2070	4170	6450
2	A	900	2780	3900	6700
	B	820	2910	3660	6750
	C	780	3120	3360	6650
	D*	853	2850	3850	6700
3	A	1120	2860	3260	6230
	B	1250	2770	3160	5970
	C	1290	2800	3200	5960
	D	1240	3200	2900	6240
4	A	870	2710	3600	6350
	B	1070	2350	3600	6270
	C	1070	1920	3920	5970
	D	1180	2410	3830	6380
5	A	880	1100	3120	4210
	B	910	910	3130	4100
	C	720	980	3240	4140
	D	980	1031	3380	4320
6	A	840	1840	2750	4600
	B	1080	1780	2590	4430
	C	1080	1770	2720	4530
	D	1180	1980	2810	5090
7	A_c	890	3030	3020	5640
	B_c	930	3110	2920	5620
	C_c	1360	2480	3270	5550
	D_c	1795	1900	3630	5500
8	A_c	1280	2020	3060	5380
	B_c	1250	2240	3330	5540
	C_c	1400	2210	3390	5520
	D_c	1300	2180	3410	5590

Legend for Table 7-1

A - Sea Level - Air - No suit - Average of 24 determinations

B - Altitude - 100% 02 - No suit - Average of 21 determinations

C - Altitude - 100% 02 - Suited - Average of 39 determinations

D - Sea Level - Air - Suited - Average of 18 determinations

A_c and B_c - Sea Level - Air No Suit

C_c and D_c - Sea Level - Air - Suited

* As explained in test data for this subject had to be discarded.

This line is the mean of three determinations made after confinement.

TABLE 7-2

MEAN LUNG VOLUMES (LITERS BTPS) OF TEST AND CONTROL SUBJECTS

	TV		ERV		IC		VC	
	Control	Test	Control	Test	Control	Test	Control	Test
Sea Level	N 46	N 146	N 46	N 146	N 46	N 146	N 46	N 146
Air - No suit	1085	945	2625	2285	3040	3388	5510	4728
Alt.-100% O_2	N 42	N 126	N 42	N 126	N 42	N 126	N 42	N 126
No suit	1090	988	2675	2215	3125	3278	5580	5610
Alt.-100% O_2	N 78	N 216	N 78	N 216	N 78	N 216	N 78	N 216
Suited	1380	957	2345	2102	3300	3380	5535	5560
Sea Level - Air	N 36	N 93	N 36	N 93	N 36	N 93	N 36	N 93
Suited	1565	1069	2040	2257	3520	3423	5545	5863

TABLE 7-3

FUNCTIONAL RESIDUAL CAPACITIES

LITERS BTPS

SUBJ.	1	2	3	4	5	6	7	8	
	3.9	5.0	3.3	2.8	2.3	2.6	4.0	4.1	
	3.9	5.0	3.3	2.9	2.3	2.6	3.8	3.9	
	3.9	5.0	3.5	2.9	2.5	2.6	3.9	3.9	
	3.9	5.0	3.5	2.9	2.4	2.7	4.2	3.9	
	4.0	5.0	3.5	2.9	2.3	2.6	4.1	3.7	
	3.92	5.00	3.42	2.88	2.36	2.62	4.00	3.89	MEAN

TABLE 7-4

SINGLE BREATH CO DIFFUSING CAPACITIES

	TEST SUBJECTS						CONTROL SUBJECTS	
	1	2	3	4	5	6	7	8
Sea Level Air	37.1*	31.2	33.9	30.8	29.7	25.9	42.7	42.0
Pre-Chamber	32.9	38.4	35.0	29.2	29.7	27.8	34.7	42.0
No suit	32.9	41.5	42.5	37.0	28.8	28.4	38.6	45.3
Sea Level Air	38.6	33.0	38.2	33.4	33.2	30.8	-	-
Pre-Altitude	43.1	40.4	33.9	33.9	29.2	27.0	-	-
No Suit	43.2	40.0	29.5	31.9	28.6	29.8	-	-
Post Altitude	35.0	33.6	30.0	30.4	27.8	28.0	35.6	43.2
Sea Level Air	38.4	35.6	32.5	26.2	27.7	32.2	39.2	-
Suited	36.2	35.5	33.4	31.1	31.1	34.5	32.5	38.8
Mean	37.5	36.6	34.3	31.5	29.5	29.4	37.2	42.3

*Carbon monoxide diffusing capacities expressed in ml of CO per minute per millimeter of mercury pressure.

TABLE 7-5

ARTERIAL BLOOD GASES & pH

Subject	pH	pO_2	PCO_2
1	7.42	670 mmHg	34 mmHg
2	7.45	684	32
3	7.47	688	27
4	7.47	676	34.2
5	7.46	679	32.8
6	7.47	640	27
7	7.43	680	36
8	7.48	684	25.6